



NBME EXPLANATIONS

NBME 21 Block 1

from CrackNBME

21-Block 1

Q1

A 24-year-old man with a history of drug abuse has nausea, rhinorrhea, hypertension, and tachycardia. The most likely cause is withdrawal from which of the following agents?

- A. Alcohol
- B. Amphetamine
- C. Cocaine
- D. Heroin
- E. Nicotine

▼ Explanation

• Answer is D (Heroin)

◦ IMP Clues:

- History of drug abuse (okay, so we know this is either an overdose or withdrawal Q)
- Rhinorrhea (Seals the deal)
- Hypertension & Tachycardia (sympathetic stimulation)

• Dx → Heroin withdrawal

- Heroin is an **opioid**.
 - Metabolized into *morphine* in CNS → **mu-opioid receptor agonism**
 - Causes: **Parasympathetic activation / Sedation**
- Overdose → coma, respiratory depression, **pinpoint pupils**
- Withdrawal → **rhinorrhea, lacrimation, piloerection, Tachycardia, HTN**, Nausea, vomiting, and diarrhea

? How does Heroin overdose affect the A-a gradient?

▼ Answer

No Change (N=10) - Opioids, Barbiturates, and Benzodiazepines cause respiratory depression so less air in alveoli = less air in arterial blood.

Increased A-a gradient is caused by agents that affect gas diffusion like fibrosis

▼ Other Choices

• Choice A → Alcohol

- MOA: **Activates GABA-A receptor** activity & **inhibits NMDA receptor** activation ⇒ **CNS Depression**
- Overdose: **CNS depression**, ataxia, slurred speech, respiratory center depression.
- Withdrawal (depends on timing, not strict though):
 - **12-48hrs (Alcoholic Hallucinosi**s): **Tactile** (bug crawling on skin) or **Visuals** (bugs crawling on walls) **Hallucinations**
 - **48-96hrs (Delirium Tremens)**: **HTN, Tachycardia**, Tremulousness, **seizures**, diaphoresis, and restlessness

• Choice B → Amphetamine

- MOA: **increases release of catecholamines** → massive **sympathetic stimulation** (similar presentation as cocaine)
- Overdose: Mydriasis, agitation, **hypertension**, insomnia, tactile hallucinations
- Withdrawal: Depression, hypersomnia, increased appetite, and anhedonia (cannot feel joy)

• Choice C → Cocaine

- MOA: **reuptake inhibition of catecholamines** → **Massive sympathetic activation** → **severe vasoconstriction**
- Overdose: **Mydriasis, Tachycardia, Hypertension**, and paranoid delusions
- Withdrawal: Severe depression & **suicidal ideation**, hypersomnia, and increased appetite



Cocaine is a USMLE favorite!

The massive surge in sympathetic stimulation causes **severe HTN** that causes **rupture of the lenticulostriate arteries of the basal ganglia**, causing an **intracranial hemorrhage**.

- Other HY Complications are **MI, Aortic dissection**, and **Nasal septum perforation**.

• Choice E → Nicotine (LY)

- MOA: **Nicotinic ACh Receptor agonist**
- Overdose: not assessed on the USMLE

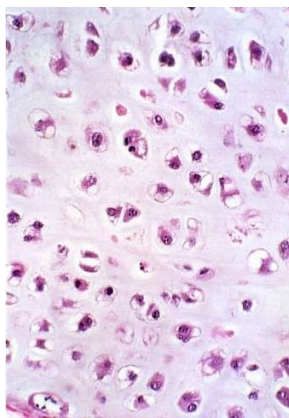
- Withdrawal: Anxiety, depression, difficulty concentrating, and weight gain

? Man had a road traffic accident and underwent surgery. 2 days later, he developed hypertension, tachycardia, and seizures. What is the cause of the above presentation?

▼ **Answer**
Alcohol Withdrawal

Q2

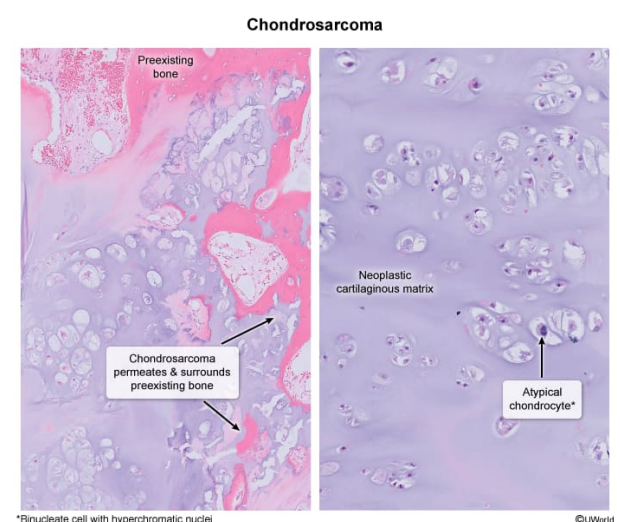
A 45-year-old man comes to the physician because of progressively worsening, constant pain in his left thigh over the past 3 months. He is a long-distance runner. An x-ray of the femur shows thickening of the diaphysis and disruption of the cortex with focal areas of increased calcification. A glistening mass containing several cysts is surgically excised. A photomicrograph of tissue from the mass is shown. Which of the following is the most likely diagnosis?



- A. Atypical stress fracture
- B. Chondrosarcoma
- C. Enchondroma
- D. Ewing sarcoma
- E. Giant cell carcinoma
- F. Multilobulated bone cyst
- G. Osteosarcoma

▼ **Explanation**

- **Answer is B (Chondrosarcoma)**
 - **IMP Clues:**
 - Diaphysis
 - Calcification
 - Glistening mass containing cysts
 - Pic shows chondrocytes (know the pic)
 - **Dx → Chondrosarcoma**
 - Site: **Diaphysis**
 - X-Ray: **Osteolytic** "moth-eaten appearance" and **Calcifications** "popcorn appearance"
 - Biopsy: **Lobules filled with chondrocytes**



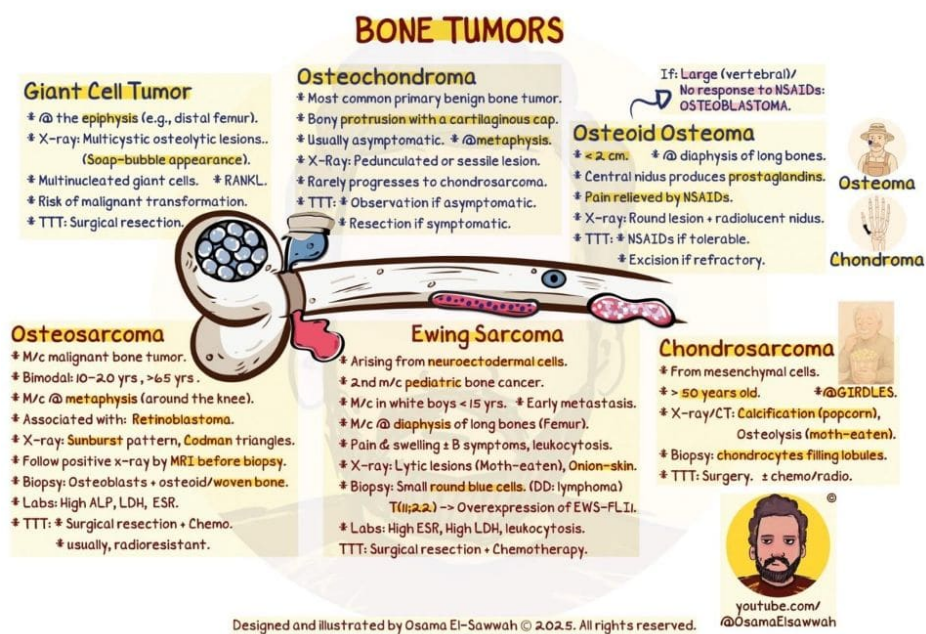
📌 The picture in the Q stem repeats on NBMEs, so know the picture!

- It is just **atypical chondrocytes** in cartilage matrix

▼ **Other Choices**

- **Choices C, D, E, G → Bone Tumors** (Ewing - Giant cell - Osteosarcoma - Enchondroma (same as chondroma))

(Credit Dr. Osama ElSawwah) "Watch the video, it's great" ([link](#))



? Patients with osteosarcoma usually have history of what other tumor?

▼ Answer

Retinoblastoma

- **RB1 gene mutation** causes Retinoblastoma & Osteosarcoma
 - RB1 gene produces *Retinoblastoma (Rb) protein* that regulates G1 → S phase (*tumor suppressor gene*)

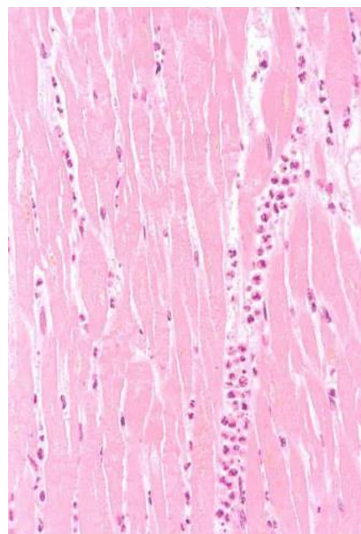
What's another tumor suppressor gene that regulates G1 → S phase?

- **p53**

- **Choices A and F** → Atypical stress fracture & Multilobulated bone cysts are just **distractors**, never saw them as the right answer.

Q3

A 50-year-old man is found dead in bed at home. His family states that he had chest pain for 3 weeks prior to his death. At autopsy, examination shows severe atherosclerosis of all three major coronary arteries, with myocardial softening and mottling involving the anterolateral wall of the left ventricle. A photomicrograph of a section from this area is shown. Which of the following is the most likely mechanism of death?



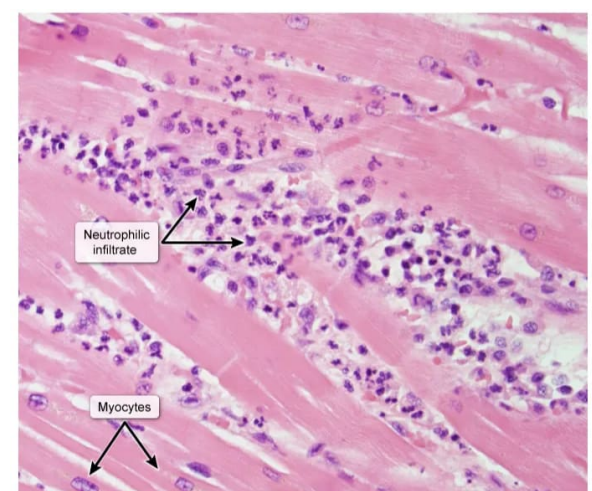
- A. Arrhythmia
- B. Cardiogenic shock
- C. Myocardial rupture
- D. Papillary muscle dysfunction
- E. Reperfusion injury

▼ Explanation

- Answer is A (Arrhythmia)
 - We know the man had an MI (chest pain - atherosclerosis - myocardial softening & mottling) so to determine which complication caused his death, **timing is key**
 - Same picture in FA: **Early Coagulative Necrosis (3-24hr post-MI)**:
 - **Most common cause of death in first 24-48hrs is Arrhythmia**

What's HY to know regarding the microscopic findings post-MI is the following:

- **0-4 hours** ⇒ **NO CHANGES**
- **4-24 hours** ⇒ Myocytes become elongated and wavy THEN hypereosinophilic with pyknotic nucleus
- **1-3 days** ⇒ **Coagulative Necrosis (no nucleus & striations) with neutrophilic infiltration**
- **3-7 days** ⇒ **Macrophages Infiltrates**



- 7-10 days ⇒ Beginning of granulation tissue formation
- 10-14 days ⇒ Well-developed granulation tissue with neovascularization
- **2-8 weeks** ⇒ **Collagen deposition & scar formation**

▼ Other Choices

- **Choice B → Cardiogenic shock on the USMLE will present as:**

- **Arrows Q: LOW CO - HIGH SVR - HIGH PCWP**

- **Low CO** → due to LV cannot pump out the blood
- **High SVR** → due to reflex mechanism (low CO is faced by a reflex mechanism causing peripheral arteriolar vasoconstriction to maintain blood pressure)
- **High PCWP** → due to blood accumulating in the LV → back up pressure to LA → high PCWP

- **Choice C → Myocardial Rupture (aka Ventricular free wall rupture)**

- Time: 5-14 days post-MI
- Wall rupture → **Acute cardiac tamponade** → **Sudden Death**

- **Choice D → Papillary muscle dysfunction (aka Papillary muscle rupture)**

- Time: 2-7 days post-MI
- Papillary muscle rupture → **Acute mitral regurgitation** → acute left side HF (**cardiogenic shock**) → pulmonary edema



Posteromedial Papillary muscle rupture > anterolateral papillary muscle rupture.

- Posteromedial has **single** blood supply → **PDA**
- Anterolateral has **dual** blood supply → **LAD & LCX**

- **Choice E → Reperfusion Injury**

- Time: 0-24 hours
- Ischemia causes accumulation of metabolites → reperfusion → Ca & ROS enters cells → **hypercontraction of myofibrils (appear as dark eosinophilic stripes)**



Patient had chest pain + dyspnea + SOB. He was managed appropriately. 3 days later, he returned to ER with dyspnea on rest. Auscultation reveals a systolic murmur. What is the cause of patient's symptoms?

▼ Answer

Papillary muscle rupture - this resulted in **acute MR** that caused **pulmonary edema**.

Made the Q vague by just saying a "systolic murmur" not the full murmur description to assess that you know that MR is a possible & HY complication of MI

Q4

A 70-year-old woman is found to have persistent fever despite intravenous broad-spectrum antibiotic therapy 3 days after undergoing operative excision of the anterior pelvic organs for recurrent cervical carcinoma. Her temperature is 38.5°C (101.3°F). Physical examination shows the presence of a central venous catheter that was placed on the day of the operation. There is also a well-healing abdominal wound without erythema and with two drains in place. Blood cultures and cultures of the tip of the central catheter on a sheep blood agar plate grow the organism shown in the photograph. A Gram stain of one of the colonies shows 4-µm, elliptical, purple, budding organisms. Which of the following is the most likely causal organism?



- A. *Candida albicans*
- B. *Cryptococcus neoformans*
- C. *Escherichia coli*
- D. *Sporothrix schenckii*
- E. *Staphylococcus aureus*

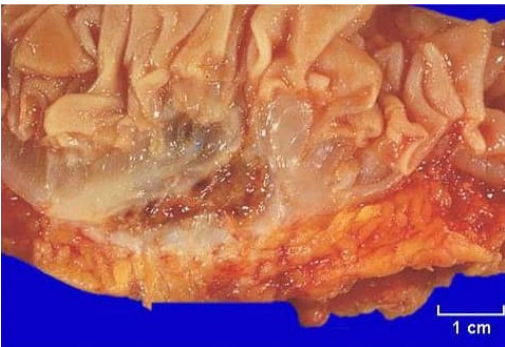
▼ Explanation

- Answer is A (Candida)
 - IMP Clues:
 - Persistent fever despite IV abx (probably not bacterial)
 - Central venous catheter (risk factor for systemic candida)
 - Purple (candida stains gram +ve),
 - Pic shows no hemolysis
 - Dx → Candidemia
 - Easy, yet tricky Q.
 - Candida is part of the normal flora on our skin, that **upon weakened immunity** (like here the patient has cervical carcinoma and is hospitalized) becomes **pathogenic**, causing:
 - **Candidemia/Disseminated Candidiasis Infection**
 - Risk Factors include:
 - **Immunosuppression** (HIV/Neutropenia/Cancer/Immunology Drugs)
 - **Diabetes**
 - **Broad-Spectrum abx use**
 - especially in patients with **central catheters** (like this patient here)
 - USMLE likes the following buzzy phrases, "*Germ Tubes*," "*budding yeast with pseudohyphae*"



Q5

A 66-year-old woman comes to the physician because of fever, chills, and left lower abdominal pain for 1 day. She has had increasingly severe constipation over the past 5 years. A barium study of the lower gastrointestinal tract shows three separate, poorly delimited regions of narrowing of the lumen of the distal sigmoid. A photograph of one of the lesions in the resected large intestine is shown. Which of the following is the most likely diagnosis?



- A. Angiodysplasia
- B. Diverticulitis
- C. Granulomatous colitis
- D. Ischemic colitis
- E. Ulcerative colitis

▼ Explanation

- Answer is B (Diverticulitis)
 - IMP Clues:
 - 66years + increasingly severe constipation over past 5 years (old & constipated)
 - Fever & chills (so some sort of -itis)
 - Left abdominal sided abdominal pain (helps us with DD and excluding choices)
 - Separated lesions (so not UC as it is continuous)
 - Sigmoid (**MC site of diverticulitis**)

◦ Dx → Diverticulitis

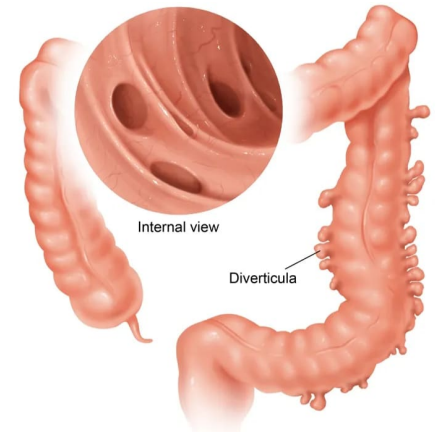
▪ First, we need to understand the “spectrum of diverticular diseases”.

• **Diverticular disease** is the mere presence of out pouches within the colon.

- Out pouches are caused by **increased intraluminal pressure** (constipation - chronic straining - low fiber diet - high meat diet) **[asked on NBME]**
- When pressure increases, mucosa looks for weak points within the colon musculature. What are these weak points? They are the **entry sites of the vasa vasorum**. **[asked on NBME]**
- What is the most common site? **Sigmoid (Left Colon)**.

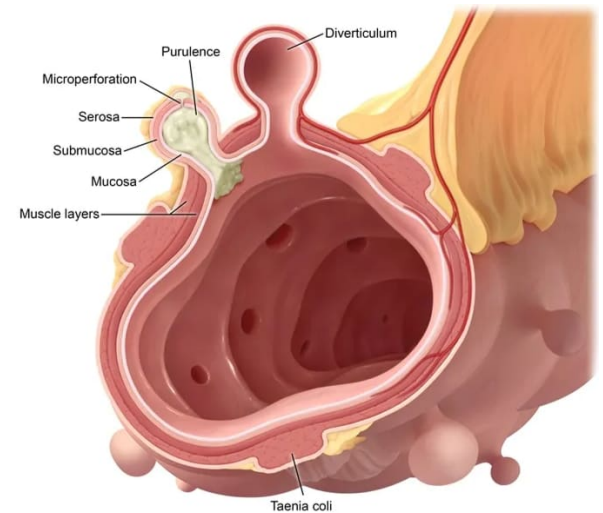
▪ **Why?**

- **Narrow & thick musculature so higher intraluminal pressure.** Easy right?

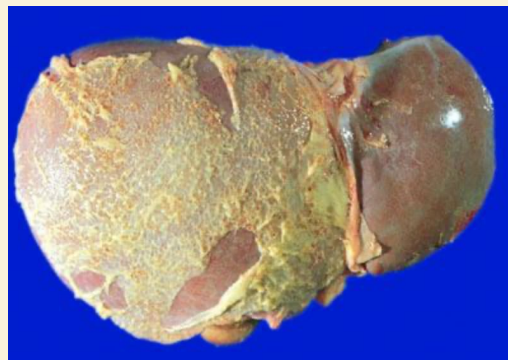


• **Diverticulitis** is the inflammation of the mucosal out pouches.

- Retained food within these pouches + bacterial growth causes infection / inflammation
 - “-itis” will cause fever & chills
- **Severe Left sided abdominal pain** (location of sigmoid colon)
- What’s the worst that can happen? **Perforation → Peritonitis → Septic shock**. Yikes.



? Patient with ruptured diverticulitis developed septic shock & death. Autopsy shows the below pic. What is the main component of the below material?

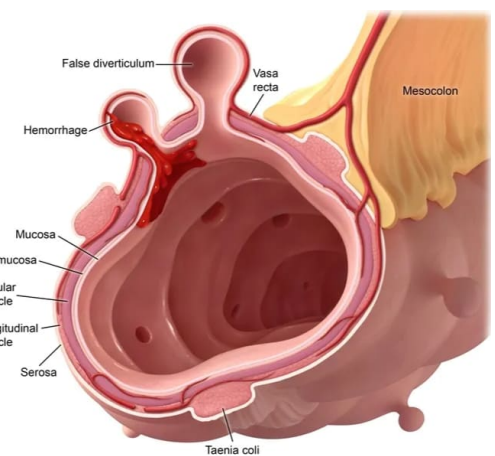


▼ Answer
Fibrin

• **Diverticular Bleeding** is bleeding caused by the diverticular out pouches compressing the vasa vasorum, causing their ischemia, perforation, and bleeding.

- **Fresh Red color** as it is a Lower GI bleed (Bleeding Per Rectum)

VS Melena/black stools of Upper GI Bleeding



▼ Other Choices

• **Choice A → Angiodysplasia**

- Presents as severe **PAINLESS** rectal bleeding (usually bright red) in an old patient
- **NO** fever or chills

? What is Heyde's Syndrome?

▼ Answer

Aortic Stenosis + Angiodysplasia

- Presents as **Aortic Stenosis** (ejection systolic murmur best heard at base of heart that radiates to carotids) + **Painless** bleeding per rectum.
- Aortic stenosis causes shearing forces that break the larger vWF multimers, causing their exposure to ADAMTS13, a metalloproteinase that cleaves vWF, causing acquired vWF diseases or bleeding tendencies (in the form of dilated capillaries in the intestines, the angiodysplasia)

USMLE will ask you what the diagnosis is/what is expected to be found on lower GI endoscopy/Why this happens?

• Choice C → Granulomatous colitis (aka Crohn's)

- Named Granulomatous due to the presence of **noncaseating granulomas** on biopsy
- **Right LQ** abdominal pain (not left) due to affection of *ileum* / *cecum*
- Causes **diarrhea** (may or may not be bloody) **NOT** constipation

• Choice D → Ischemic colitis

- Present as **diffuse** severe abdominal pain +/- bleeding
- **NO** fever / chills
- Usually caused by an **embolus occluding SMA / IMA or atherosclerosis**
- HY Underrated Risk Factor on the USMLE is **AF**
 - Presents as a **patient with AF** that develops **acute severe abdominal pain + mild tenderness on palpation +/- bleeding per rectum**

The concept of "**pain that exceeds severity physical findings (tenderness)**" is super buzzy for Ischemic Colitis.

• Choice E → Ulcerative Colitis (UC)

- Present as **bloody diarrhea** (**NOT** constipation)
- **Left** Sided abdominal pain (due to involvement of rectum / sigmoid colon)
- **Continuous** lesions (**NOT** separated)

? Can you mention 6 HY differences between Crohn's & Ulcerative Colitis?

▼ Answer

Crohn's Disease

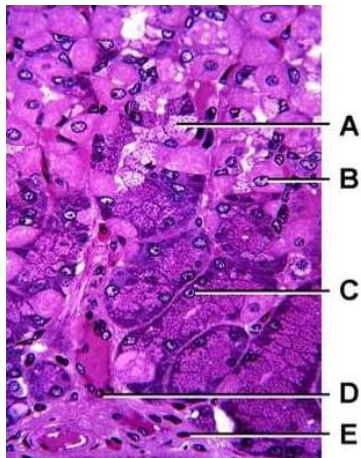
1. Terminal Ileum + Cecum affection with rectal sparing
2. Transmural Inflammation
3. Cobblestone mucosa + skip lesions
4. Noncaseating granulomas
5. Fistula is major complication
6. String Sign

Ulcerative Colitis

1. Colon (most commonly sigmoid) with rectal affection almost always
2. Mucosal & submucosal inflammation
3. Friable ulcerated mucosa + continuous lesions
4. Crypt abscess
5. Toxic Megacolon is major complication
6. Lead pipe sign

Q6

A 51-year-old woman comes to the physician because of a 6-month history of burning abdominal pain that occurs 1 to 2 hours after eating. She sweats profusely and has light-headedness when she stands. Her blood pressure is 105/70 mm Hg while standing. Physical examination shows epigastric tenderness. A CT scan of the abdomen shows a 2-cm mass on the proximal duodenum. Gastrin released by the tumor cells stimulates which of the following labeled cells in the photomicrograph shown to release hydrogen ions?



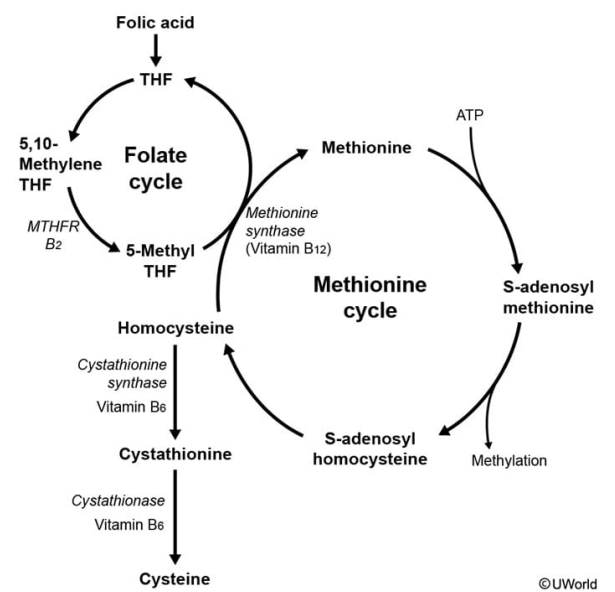
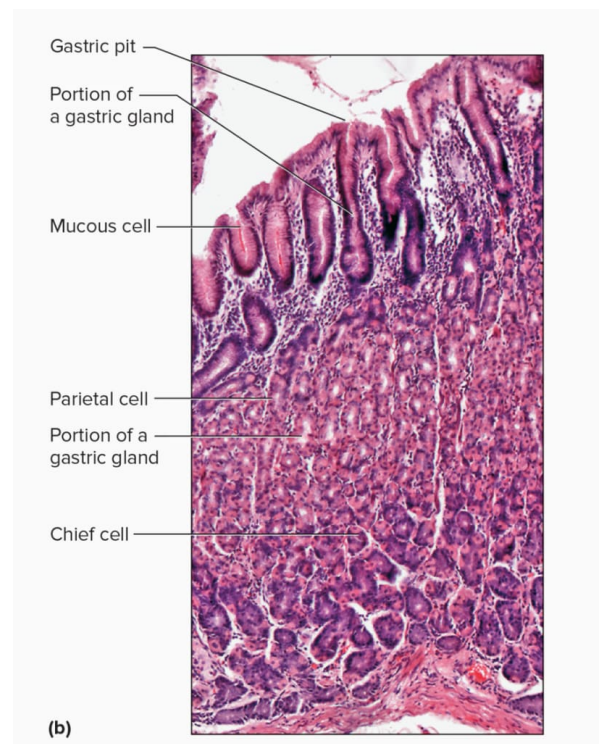
- A. A
- B. B
- C. C
- D. D
- E. E

▼ Explanation

- The answer is B
 - Overall, histology is very LY on the USMLE. However, this picture shows up quite a bit so know it.
 - Q asks gastrin stimulates which cells to produce H ions (aka HCL aka gastric acid) → **Parietal Cells**
 - **Parietal cells are Pink (eosinophilic) and have 2 functions:**
 1. **Produce HCL** which can activate pepsinogen to pepsin via stimulation of gastrin from G cells
 2. **Secretes Intrinsic Factor** which binds to vitamin B12 to facilitate absorption in terminal ileum

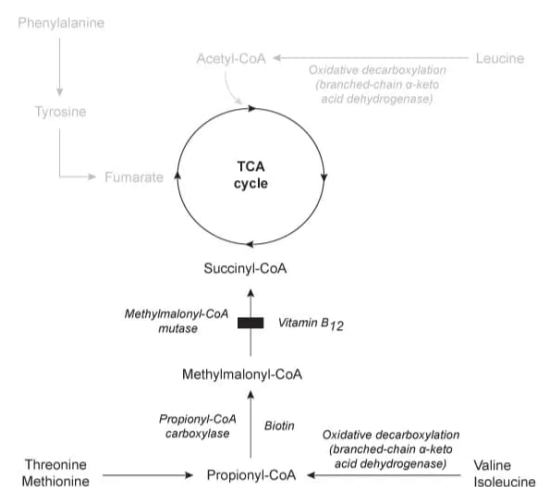
Destruction of parietal cells or deficiency of Intrinsic Factor → Pernicious Anemia

- **Vitamin B12 deficiency** is the most assessed sequelae of pernicious anemia, let's go over how it presents:
 - **Hematological complications** → Macrocytic anemia (MCV > 100)
 - **Neurological complications** → Subacute combined degeneration
 - **Psychological complications** → depression, psychiatric symptoms
 - **Biochemical complications:**
 - Homocysteine metabolism:
 - **Homocysteine → Methionine** via **Methionine synthase** which require **vitamin B12**.
 - Vitamin B12 deficiency causes: **increased Homocysteine & decreased Methionine**
 - **Increased homocysteine causes increased risk of atherosclerosis & thrombosis**
 - Fatty Acid Metabolism:
 - **Methylmalonyl-CoA → Succinyl-CoA** via **Methylmalonyl-CoA mutase** which requires **vitamin B12**.
 - Vitamin B12 deficiency causes **accumulation of methylmalonic acid**
 - **Increased methylmalonic acid is toxic to myelin, causing Subacute Combined Degeneration**



Homocysteine & Methylmalonic acid in vitamin B9 vs vitamin B12

- Vitamin B12 → **HIGH** Homocysteine & **HIGH** Methylmalonic acid
- Vitamin B9 → **HIGH** Homocysteine & **NORMAL** Methylmalonic acid



? What are the affected components of Subacute combined degeneration?

▼ Answer

1. **Dorsal Column**
2. **Spinocerebellar Tract**
3. **Corticospinal Tract**

▼ Other Choices

- Nonsense histology. What you need to know is parietal cells (**Choice B**) the pink cells & chief cells (basophilic cells).
- **Chief Cells (Choice C)**
 - Produces **pepsinogen** which is activated by HCL (secreted by?? Parietal cells yes.) into pepsin which digests protein
- Not really sure about the other options (I am not a histologist neither interested in histology) but I think **choice A** is mucus neck cells that secrete mucus?
- No idea what **choices D & E** are.

Q7

A 65-year-old man dies in a motor vehicle collision. A photograph of a lung as seen at autopsy is shown. Which of the following is the most likely diagnosis?



- A. Abscess
- B. Hamartoma
- C. Infarct
- D. Malignant lymphoma
- E. Mesothelioma
- F. Squamous cell carcinoma

▼ Explanation

- Answer is F (SCC)
 - **IMP Clues:**
 - Pic tells it all: **CAVITATION = SCC (KNOW THIS WELL)**
- **Dx → Squamous Cell Carcinoma (SCC) of the Lung**
 - **Central mass** that mostly affects **smokers** with cavitation
 - Origin = Epithelial cells
 - Biopsy shows **Keratin pearls (like any other SCC) + stains positive for Keratin**
 - Associated with **"Cavitations"** on the USMLE
 - Releases **PTHrP** → **Hypercalcemia**
 - USMLE may convey this as renal stones in a patient with hemoptysis & weight loss

? Patient with SCC. Arrows of PTH, Calcium, Phosphate?

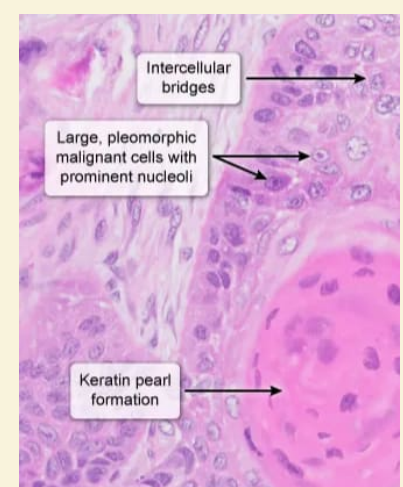
▼ Answer

- **LOW** PTH
- **HIGH** Calcium
- **LOW** Phosphate

PTHrP is not the same as PTH. It does its job yes, but it is not the same molecule. Calcium is increased & Phosphorus is decreased. This cause PTH to go down.

▼ SCC Pics:

- Keratin Pearls:

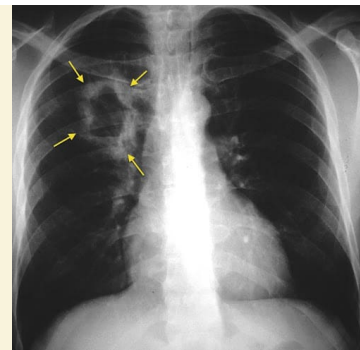


- Cavitation on CXR:



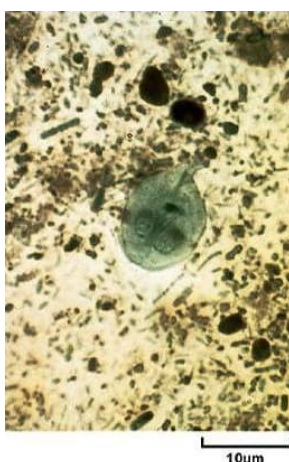
"SSSS"

Sentral (Central) lung cancers are Small cell carcinoma & Squamous cell carcinoma and are associated with Smoking.



Q8

A 22-year-old man comes to the physician because of a 2-month history of foul-smelling, watery diarrhea with significant flatulence; he also has had a 4.5-kg (10-lb) weight loss during this period. He recently returned from a trip to rural Indonesia, where he did not always have access to clean water. He appears thin. Physical examination shows a soft, mildly distended abdomen with active bowel sounds. A photomicrograph of a stool specimen is shown. The most appropriate pharmacotherapy has which of the following mechanisms of action?



- A. Enhancement of cell membrane permeability to chloride ions
- B. Formation of destructive free radicals
- C. Inhibition of DNA polymerase
- D. Inhibition of protein synthesis
- E. Prevention of microtubule assembly

▼ **Explanation**

- **Answer is B (Formation of destructive free radicals)**

- **IMP Clues:**

- Foul-smelling watery diarrhea with flatulence + weight loss
- Hx of travel with no clean water. Cmon. Classic Giardia vignette
- This is Giardia, you should know this picture.

- **Dx → Giardia Infection**

- Treatment of Giardia is **Metronidazole**

- **MOA: Produces an active metabolite that destroys DNA via free radicals**

- USMLE like to present giardia as "people who went camping & drank unclean water + now have **steatorrhea** (foul smelling bulky greasy loose stools that float)" [These keywords are buzzy & mentioned in almost all cases of giardia]

- They can also be tricky & mention travel to a country (like Indonesia/Honduras) where they drank tap water and then, developed loose stools that floats.
- Giardia **doesn't** cause fever or vomiting

- Stool microscopy would show the **trophozoites**:



Giardia **DOESN'T** invade the intestinal mucosa, but **attaches** to it, causing **blunting of villi** ⇒ **Malabsorption** & **Hindering of brush border enzymes**





- ⚠ USMLE loves to mention giardia in vignettes of patients with **IgA deficiency** or **X-Linked Agammaglobulinemia**.
- Both have IgA deficiency → **decreased mucosal immunity**

- ? **How is Giardia diagnosed?**
- ▼ **Answer**
Classically, **Stool Microscopy** showing the trophozoites or cysts.
However, **stool antigen testing (ELISA or PCR)** are more sensitive

▼ **Other Choices**

- Choice A** → is weird, but could possibly be Benzo or barbs?
- Choices C & D** → could be for a million different drug (DO THE MEHLMAN PHARM ANKI GUYS)
- Choice E** → is for -bendazoles (+ other microtubules inhibitors, again do the mehlman anki)

? **What are the HY drugs that relate to microtubules?**

▼ **Answer**

- Microtubule Inhibitors**
 - Colchicine
 - Albendazole & Mebendazole (-bendzoles)
 - Vincristine
 - Vinblastine
 - Griseofulvin
- Microtubules Stabilizers**
 - Paclitaxel & Docetaxel (Taxanes)

Q9

A 25-year-old nulligravid woman comes to the physician because she and her husband have not been able to conceive a child for 3 years. Previous evaluation of the husband showed no abnormalities in spermatogenesis. Menarche was at the age of 13 years. Menses occur at irregular 60- to 90-day intervals. She is 157 cm (5 ft 2 in) tall and weighs 68 kg (150 lb); BMI is 28 kg/m². Physical examination shows hirsutism. Ultrasonography shows ovaries with numerous cysts beneath the capsule. A photograph of the uterus and the ovaries from a woman with a similar condition is shown. This patient is at greatest risk for developing which of the following conditions?



- Adenomyosis
- Dermoid cyst
- Ectopic pregnancy
- Endometrial hyperplasia
- Endometriosis
- Hydatidiform mole
- Leiomyomata uteri
- Meigs syndrome
- Placenta Previa

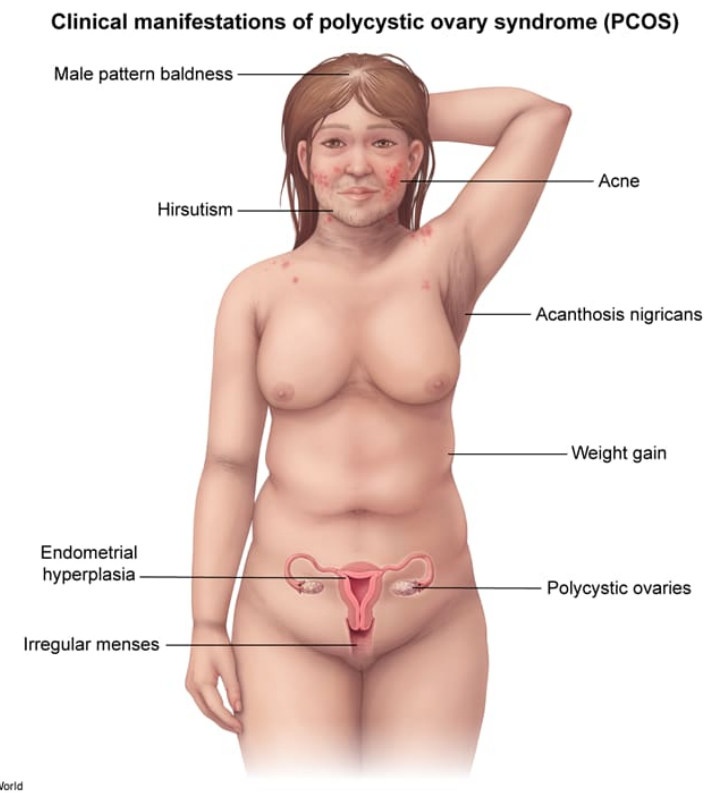
▼ **Explanation**

- Answer is D (Endometrial Hyperplasia)**
 - IMP Clues:**
 - Nulligravida (hyperestrogenic)

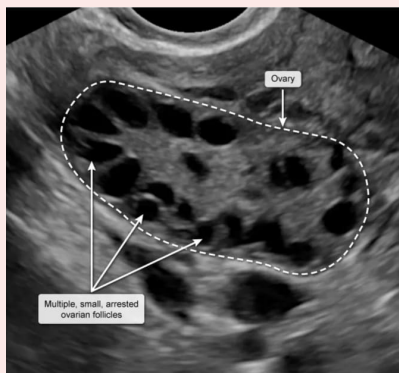
- Irregular menses (hormones are all over the place)
- BMI is 28 (a little chubby)
- Hirsutism (increased Androgen)
- Numerous cysts & the pic (multiple cysts in the periphery of ovaries, cmon man, it is PCOS)

• **Dx → PCOS**

- Non-ovulatory = no progesterone to offset the effects of Estrogen = **HYPER-ESTROGENEMIA**
 - **Unopposed estrogen = ENDOMETRIAL HYPERPLASIA**
- Characterized by Triad of:
 1. **Insulin Resistance**
 2. **High Androgen**
 3. **High LH/FSH ratio**
- Complications of PCOS
 1. Metabolic Syndrome
 2. Hirsutism (hair on upper lips, chin, chest) & **Acne**
 3. Irregular menses & Infertility
 4. **Endometrial Hyperplasia & Endometrial Carcinoma**
 - USMLE tests this concept in cases of **anovulation** (like here in **PCOS**) & cases of **unopposed hyperestrogenemia** (women on **Estrogen-only pills** or **Tamoxifen**)



USMLE can be assholes & give you **U/S of the ovaries** (below) or its **"String of Pearls Appearance"** or **"Necklace pattern"** description and ask for the diagnosis/cause/one of the above triad/arrows:



- If they ask for cause of the U/S appearance, the answer is **"chronic anovulation, causing failure of follicles rupturing"**

? On the USMLE, you will get an arrows Q with FSH & LH in PCOS. What to choose?

▼ Answer

- **HIGH LH**
- **NORMAL FSH** (yes, normal. That's what USMLE wants. Normal FSH not low)

? USMLE gives you a case of PCOS/Estrogen-Only Pills/Tamoxifen & asks what is patient at risk of developing

▼ Answer

Endometrial Hyperplasia/Carcinoma

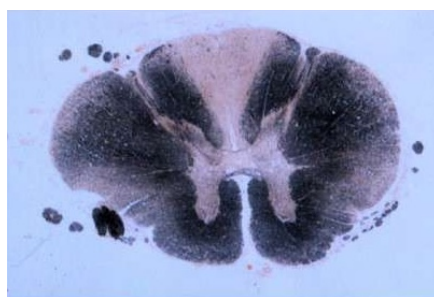
▼ Other Choices

- **Choice A → Adenomyosis**
 - Growth of the endometrial tissue within myometrium
 - Presents as pain, bleeding, and enlarged uterus (not pregnant, just diffuse enlargement of uterus)
 - In a MULTIGRAVIDA
- **Choice B → Dermoid cyst**
 - Mature cystic teratoma (contains many germ layers → hair, teeth, skin +/- calcifications)
- **Choice C → Ectopic pregnancy**
 - Present as severe pain **followed** by bleeding + not bilateral
- **Choice E → Endometriosis**
 - Growth of endometrial tissue outside the uterus (**most commonly the ovaries**)
 - Presents as SEVERE MENSTRAUL PAIN, dyspareunia, pelvic tenderness, **nodularity of the uterosacral ligament, or a fixed retroverted uterus.**
- **Choice F → Hydatidiform Moles**
 - Nonviable pregnancy that results in abnormal proliferation of trophoblastic cells (type of GTD)

- Presents as enlarged uterus > gestational age + super high B-hCG levels
 - Types → Complete, Partial, Invasive, and Choriocarcinoma
- **Choice G → Leiomyomata Uteri (Fibroid)**
 - Smooth muscle tumor of myometrium
 - A very good DD, but Fibroid would present as breakthrough bleeding + heavy menses + enlarged uterus depending on location
 - On STEP 1, most of the time it would be an incidental finding on US or autopsy & THEY WOULD NOT BE MANAGED. LEAVE IT ALONE.
 - **Stains positive for Desmin (stains muscle)**
- **Choice H → Meig's Syndrome (never seen it get assessed on the USMLE)**
 - Triad of → Benign Ovarian Fibroma + Ascites + Right sided pleural effusion
- **Choice I → Placenta Previa**
 - Placenta implants over the internal cervical os
 - Causes **painless 3rd trimester bleeding**
 - Hx of prior interventions to the uterus (myomectomy or previous C-Section) increases risk of placenta previa due to probability of abnormal implantation (Placenta loves adhering to scar tissue)

Q10

A photograph is shown of a myelin-stained cross section of a spinal cord obtained at autopsy from a 50-year-old woman. She sustained a spinal cord injury in a motor vehicle collision 15 years prior to her death. Which of the following symptoms would most likely have been present in this patient as a result of the damage indicated in the photograph?



- A. Atrophy of the arm muscles
- B. Atrophy of the thigh muscles
- C. Hyperreflexia of the quadriceps deep tendon reflex
- D. Hyperreflexia of the triceps deep tendon reflex
- E. Loss of sensation to vibration over both feet
- F. Loss of sensation to vibration over both hands

▼ Explanation

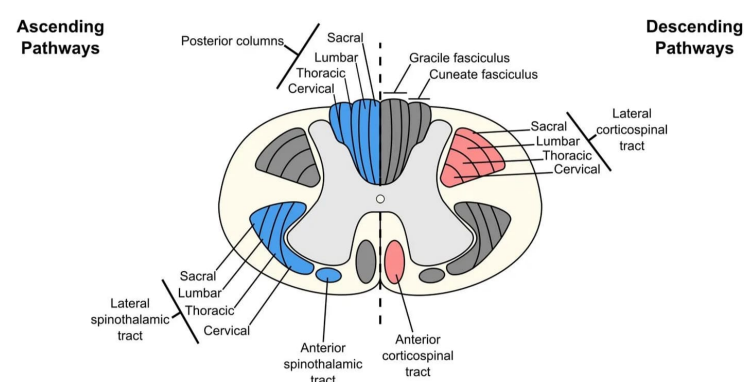
- Answer is E (Loss of sensation to vibration over both feet)

Pass-Level & VERY HY to know:

- MYELIN STAINS BLACK
- IF NOT BLACK → Unmyelinated/Demyelinated

- Dorsal column is affected & specifically the medial part (Gracile) → **Lower Limb vibration and proprioception sense**

Mnemonic I use to remember that **Gracilis is the tract for the lower limb** is that we have a **muscle called the Gracilis muscle in our legs.**





Rapid Review of HY Tracts:

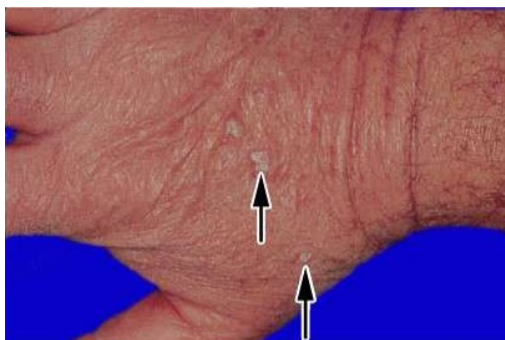
- **Gracile** Fascicles of **Dorsal Column** → **Vibration & Proprioception of Lower Limb**
- **Cuneate** Fascicles of **Dorsal Column** → **Vibration & Proprioception of Upper Limb**
- **Spinothalamic Tract** → **Pain & Temperature sensation**
- **Corticospinal Tract** → **Motor action**



Nerve fibers that convey pain & temperature sensation are NON-MYELINATED. USMLE give you an EM microscopy picture of a myelinated (surrounded by a black layer) & unmyelinated (with no surrounding black layer) with an "X" on the unmyelinated nerve. The Q then asks for function of the labeled "X" nerve. Answer was "**Conveys pain and temperature sensation**".

Q11

A 62-year-old man who is a farmer comes to the physician because of an 8-year history of the lesions indicated by the arrows shown in the photograph. Although there is no itching, he occasionally picks at the lesions, which causes some bleeding. Physical examination shows numerous similar rough plaques on the scalp, face, ears, and forearms. Which of the following is the most likely diagnosis?



- A. Actinic keratosis
- B. Basal cell carcinoma
- C. Hand dermatitis
- D. Psoriasis
- E. Seborrheic keratosis
- F. Squamous cell carcinoma
- G. Tinea corporis
- H. Verruca vulgaris

▼ Explanation

- **Answer is A (Actinic Keratosis)**
 - **IMP Clues:**
 - **Farmer** (usually the USMLE would use the "Farmer" to signify some risk factors like Sun-exposure, Fungal infections, Parasites and OPC poisoning, or tetanus.
 - Rough plaques (**V.IMP keyword**)
 - Scalp, face, ears, forearms (sun-exposed areas).
 - **Dx → Actinic Keratosis**
 - also named on the USMLE as "**Solar Keratosis**"
 - **Scaly / rough lesions with a "sandpaper feel" [buzzey description]** on **sun exposed areas**, usually found on farmers / construction workers / fishermen.
 - **Why?**
 - **Chronic UV radiation induces DNA damage in keratinocytes**, causing mutations that result in abnormal cell cycle regulations.
 - Overtime, this causes uncontrolled cell proliferation, causing **abnormal keratinocytes accumulation & formation of actinic keratosis**.



What are people with Actinic Keratosis at risk of developing?

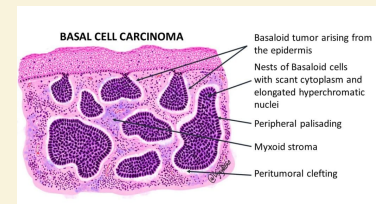
▼ **Answer**
SCC of skin.

▼ Other Choices

• Choice B → BCC

- **Pearly / slightly translucent mass with telangiectasia** (classically rolled edges)
- Origin: **Basal layer of EPIDERMIS (NOT DERMIS)** [asked on NBME]
- Biopsy: **Purple / dark blue cells with peripheral palisading and cleft formation**
- Outcome: Local growth with tissue destruction (rarely metastasizes) [asked on NBME]

BCC Pictures:



• Choice C → Hand Dermatitis is such a broad title & will be discussed later

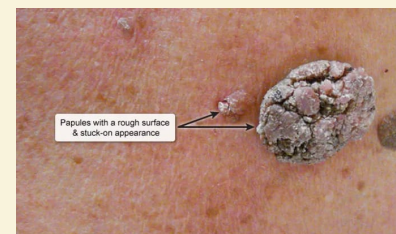
• Choice D → Psoriasis

- Site: classically on **extensors (most commonly on knee/elbows)** but can be seen on forehead & face
 - Vignettes will say a patient with **bloody diarrhea (associated UC)** + **Scales** → think psoriasis
 - May also ask about psoriatic arthritis → **Pencil-in-cup deformity**
- Associations: **HLA-B27 ("PAIR" → Psoriasis - Ankylosing Spondylitis - IBD - Reactive Arthritis)**
- **Auspitz sign:** Bleeding of scales on removal [classic sign & used in almost all psoriasis vignettes]
- **Munro micro-abscesses:** collection of neutrophils in stratum corneum of epidermis [asked on NBME]

• Choice E → Seborrheic Keratosis

- Old patient + **sun exposure**
- **Greasy waxy skin growths** with a "**stuck on appearance**" that appear as if they can be "**peeled off**" or "**about to fall**"
- Associated with **Leser-Trelat sign:** eruption of seborrheic keratosis 2ry to **visceral malignancy**

Seborrheic Keratosis Pictures:



• Choice F → SCC

- Ulcerative mass on the USMLE (with minor exceptions in vignette, seen as rolled edges)
- Biopsy: **Keratin pearls with intracellular bridges** [asked on NBME]
- Major Risk Factors: Smoking & Immunodeficiency (HIV increases incidence of all SCC)

• Choice G → Tinea Corporis

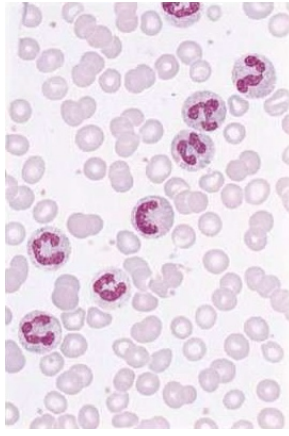
- Circular pruritic lesion with advancing edges and central clearing
- Treatment → Topical -azoles (**MOA → inhibits 14-demethylase**) [asked on NBME]

• Choice H → Verruca Vulgaris

- HPV warts on the hands (Warts. The pic does not show warts)

Q12

A 68-year-old woman has had a fever and shortness of breath for the past week. X-rays of the chest show a right lower lobe infiltrate. Leukocyte count is 38,000/mm³. A peripheral blood smear is shown. Which of the following best describes her peripheral blood smear?



- A. Acute lymphoid leukemia
- B. Acute myeloid leukemia
- C. Chronic lymphocytic leukemia
- D. Reactive granulocytosis
- E. Reactive lymphocytosis

▼ Explanation

- **Answer is D (Reactive Granulocytosis)**

- **IMP Clues:**

- Hx of infection (fever - SOB - pneumonia in the form of RLL infiltrate)
- WBC count of 38,000 (normal is 4000-11,000, you may be like "DAMN ITS LEUKEMIA" No. Look at the smear)
- Smear shows **NORMAL CELLS. (It's a leukemoid reaction).**

- **Dx → Reactive Granulocytosis or Leukemoid Reaction**

- **Elevated WBCs "released from Bone Marrow reserve pool,"** resembling Leukemia (hence the name "leukemoid")
- Caused **2ry to infection** (always look for infection source in vignette)
- Count most likely **≥30,000** (normal infections will be max 20,000s)
- **Leukocyte ALP is high**
- Smear demonstrates "neutrophilia" (lots of neutrophils)

They are normal looking WBCs with no features of malignancy.



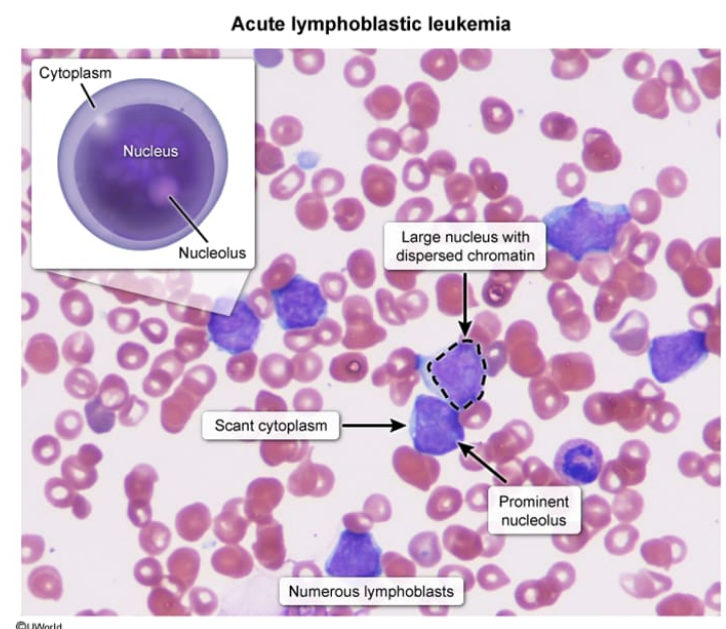
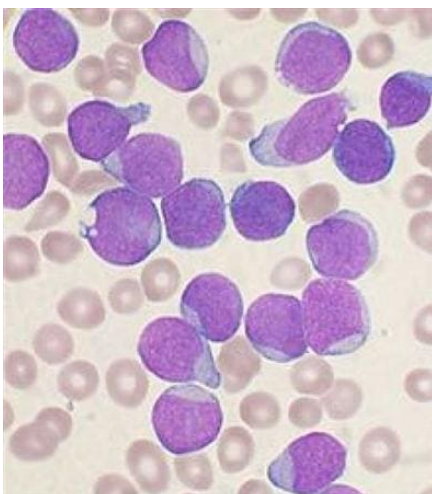
Leukocyte ALP reflects Leukocyte function.

- In **Reactive Granulocytosis**, leukocytes are increased & **functional**, hence the **elevated leukocyte ALP**.
- In **Myeloid Leukemia**, **ALP is LOW** because while there are **MANY** leukocytes, they are **non-functional**.

▼ Other Choices

- **Choice A → Acute Lymphoid Leukemia (ALL)**

- **Kid with super high WBCs (lymphocytes)**
- Increased risk with **Down Syndrome**
- Markers: **CD10 & TdT positive**
- Smear used on NBMEs:

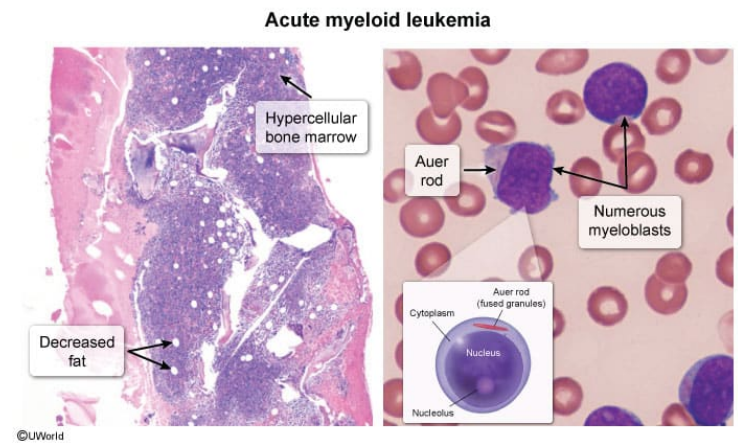
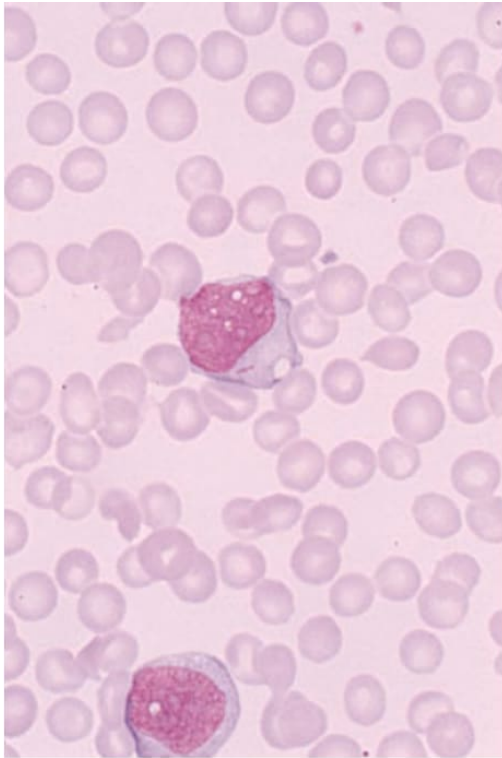


- **Choice B → Acute Myeloid Leukemia (AML)**

- **Adult** with lots of myeloid blasts
- Smear shows **Auer rods**, composed of **myeloperoxidase**

Auer rods can be liberated during ttt of AML (leukemic cell lysis) & cause DIC

- Smear used on NBMEs:

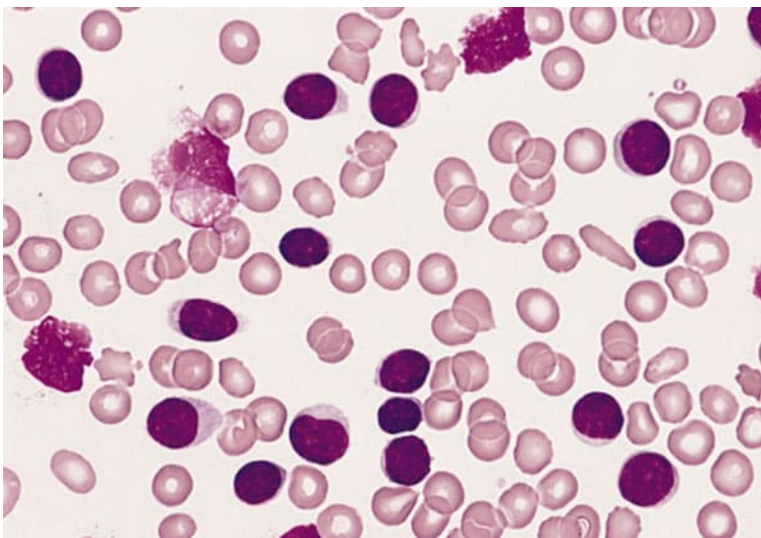


Acute Promyelocytic Leukemia "APL"

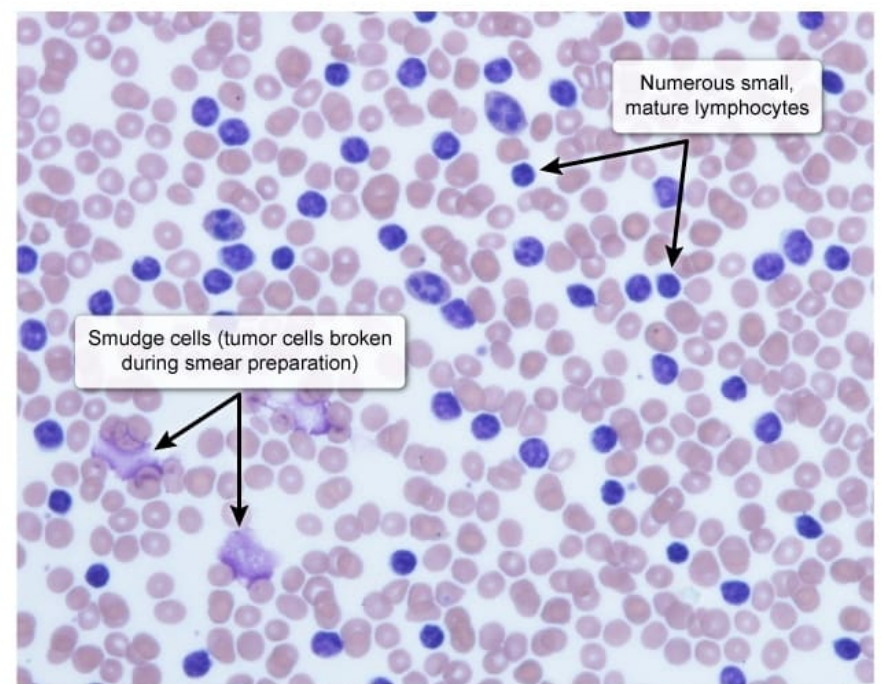
- AML type 3 is caused by a **t(15:17) translocation** that can be treated with Vitamin A
 - **Vitamin A causes maturation of blasts into mature granulocytes [asked on NBME]**

- **Choice C → Chronic Lymphoid Leukemia (CLL)**

- Usually **Elderly** with **super high WBCs (lymphocytes)**
- Markers: **CD5 & CD23**
- Associated with **Warm AHA (IgG against RBCs)**
- Smear shown on NBMEs showing smudge cells:



Chronic lymphocytic leukemia



- **Choice E → Reactive Lymphocytosis**

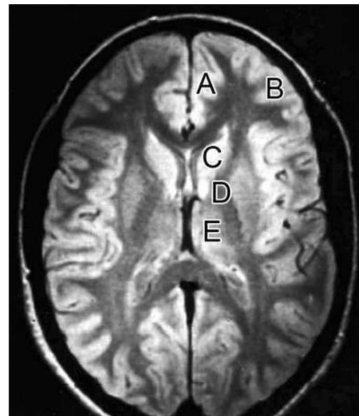
- A **child** + very high WBCs mainly **lymphocytes** (also a subset under leukemoid reaction)

Very HY differential for ALL as it presents in the same way, but differentiated by:

- Vignette will say there is:
 - **Cough**
 - **Post-tussive emesis (vomiting after cough)**
 - **Hypoglycemia**

- Mechanism: Pertussis toxin → **Inhibits Gi via ADP ribosylation** → causes **increased cAMP** → Lymphocytosis

A 43-year-old woman dies after a 10-year illness characterized by irregular jerking movements of the extremities and a disjointed gait. She had profound dementia during the last 2 years of her life. Her father had a similar disorder and died at the age of 65 years. At autopsy, examination of this patient's brain is most likely to show severe atrophy of which of the following labeled structures in the MRI of the normal brain?



- A. A
- B. B
- C. C
- D. D
- E. E

▼ Explanation

- Answer is C (Caudate Nucleus)

- IMP Clues:

- Irregular jerky movement of extremities & disjointed gait (Choreoathetosis)
 - Hx of Dementia (Neurodegeneration)
 - Family Hx of similar condition & Father died at 65y, while she died at 43 (Anticipation)

- Dx → Huntington's Disease

- AD disease characterized by **CAG TNR expansion** of **Huntingtin (HTT) gene** on **chromosome 4**.

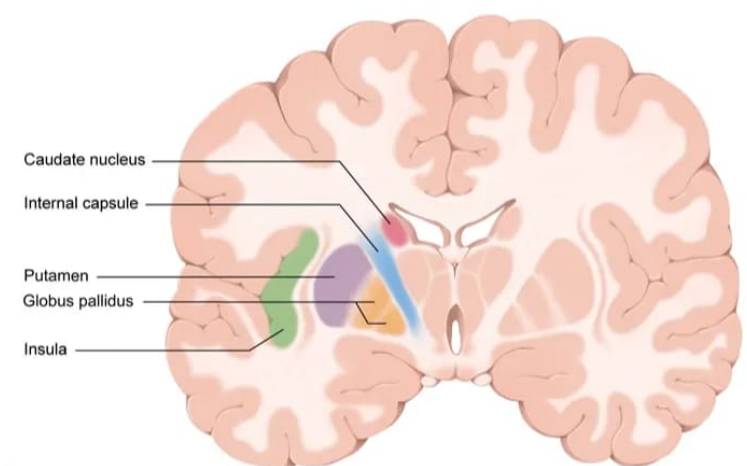
- What happens as a result?

- Accumulation of the toxic protein in the brain, with **favoring of GABA neurons & Cholinergic neurons in the stratum (Caudate nucleus & Putamen)**, causing death of neurons.

? What are the expected arrows of Ach, GABA, and Dopamine in this patient?

▼ Answer

Decreased Ach - Decreased GABA - Increased Dopamine



- Caudate Nucleus atrophy causes:

- **Choreoathetosis** (Irregular jerky movement of extremities & disjointed gait)
 - **Neurodegeneration** (Dementia)
 - "Apparent" enlargement of ventricles, causing **"Hydrocephalus Ex-vacuo"**

? Patient's grandfather had dementia + abnormal limb movements and died at 84. Patient's uncle had the same symptoms and died at 63. The doctor told the patient that he's at risk of developing similar symptoms at a younger age. What is this referred to?

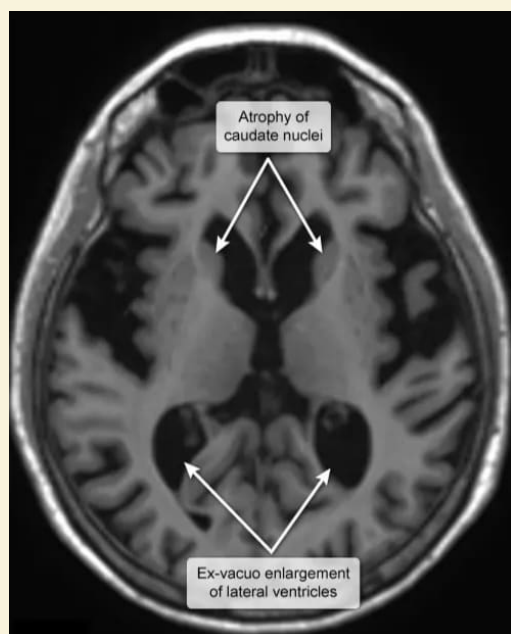
▼ Answer

Anticipation

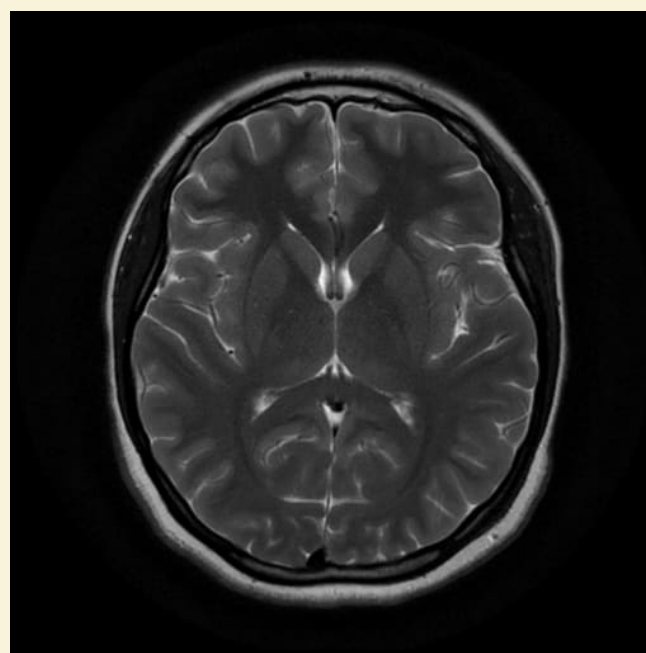


Huntington Disease Brain MRI vs Normal Brain MRI:

Huntington Disease:



Normal Brain:

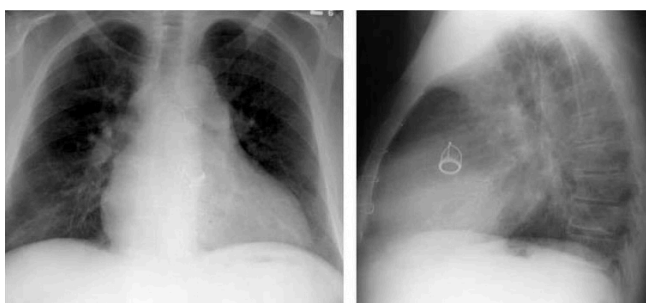


▼ Other Choices

- Confusing answers here would be:
 - **Choice D** → Internal Capsule that on the USMLE is supplied by lenticulostriate arteries & affection most likely will cause **CONTRALATERAL PURE MOTOR AFFECTION**
 - **Choice E** → Thalamus that on the USMLE if affected would cause **CONTRALATERAL PURE SENSORY AFFECTION**. It is also good to remember that VPL supplies the Body & VPM supplies the face

Q14

A 43-year-old man comes to the physician for a follow-up examination. Ten years ago, he underwent cardiac valve replacement. Chest x-rays are shown. Based on these findings, which of the following valves was most likely replaced in this patient?



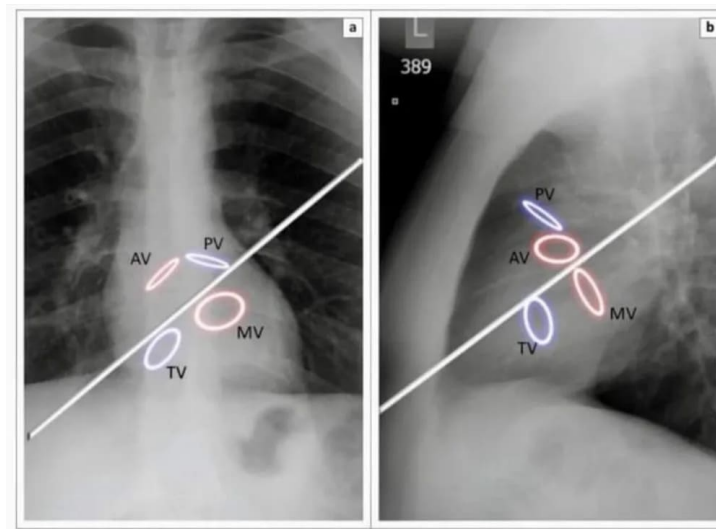
- A. Aortic
- B. Mitral
- C. Pulmonic
- D. Tricuspid

▼ Explanation

- Answer is A (Aortic)
 - There are 2 Qs in all NBMEs/Free120 testing this concept. It's LY and just garbage.
 - **Method 1:**
 - Choose **Aortic valve** as it is the most common valve replaced in general.
 - Never choose Pulmonary or Tricuspid valves. So, either **Aortic or Mitral**:
 - If patient is **OLD** → **Aortic valve** almost always
 - If patient is **YOUNG**, you can use Method number 2:

- **Method 2:**

1. Draw a line from **Right cardiophrenic angle to below Left hilum**
 - a. If **ABOVE** the line → **Aortic valve**
 - b. If **BELOW** the line → **Mitral valve**
 - c. If on the line → Uncertain (just guess aortic valve)



Q15

A 37-year-old man is brought to the emergency department 45 minutes after sustaining injuries in a motor vehicle collision. He has severe, sharp, right-sided chest pain. His respirations are 30/min and labored. Physical examination shows numerous areas of trauma to the right side of the head and thorax. Breath sounds are decreased on the right, and there is hyperresonance in the right thorax. Physical examination shows decreased tactile fremitus, and adventitious sounds are absent. X-rays confirm multiple rib fractures. A CT scan of the chest is shown. The most likely afferent pathway of this patient's chest pain is carried in which of the following nerves?

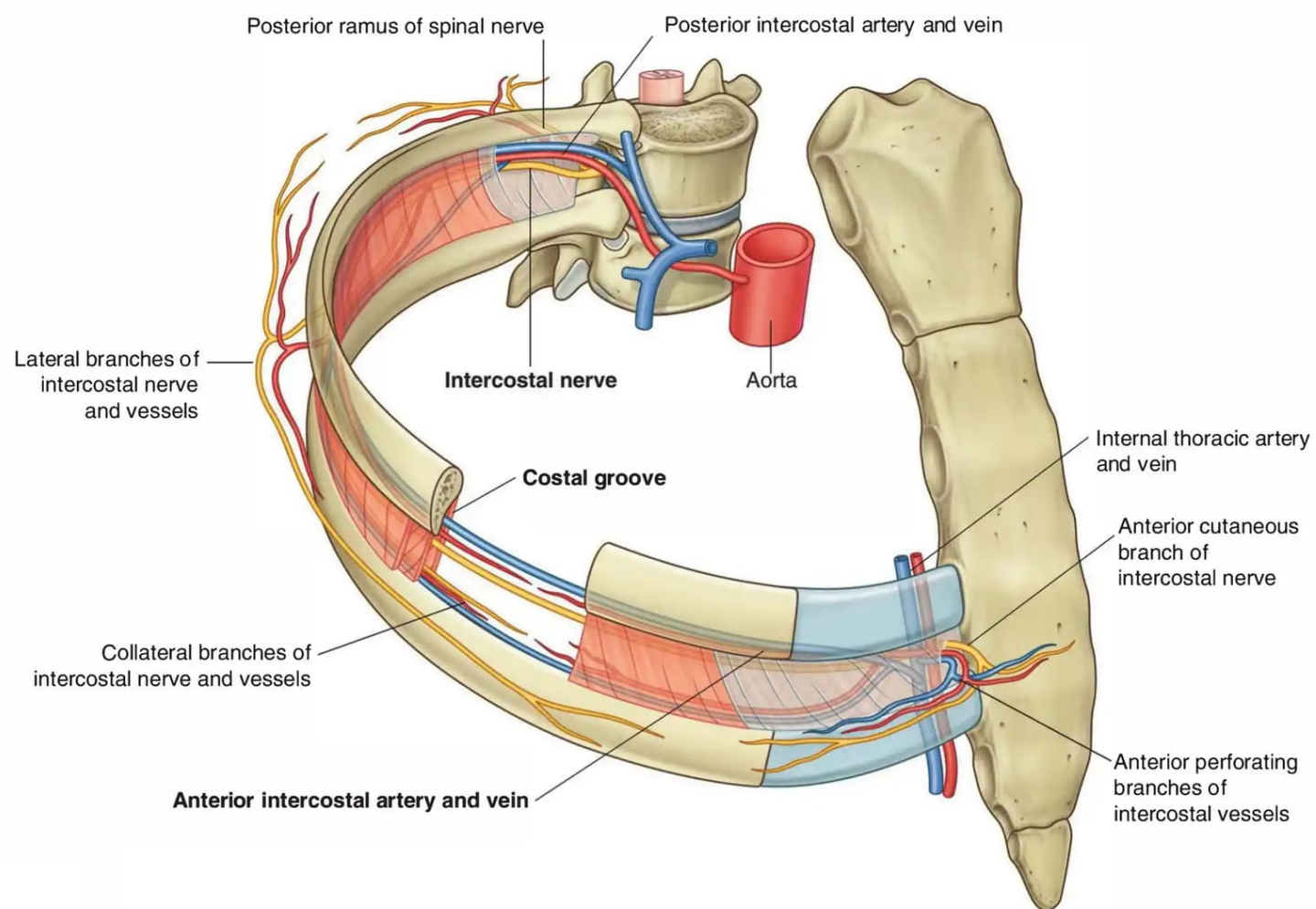


- A. Greater thoracic splanchnic
- B. Intercostal
- C. Phrenic
- D. Pulmonary parasympathetic
- E. Vagus

▼ **Explanation**

- **Answer is B (Intercostal)**
 - What USMLE wants you to know is **Chest pain caused by rib fracture is conveyed via the Intercostal nerves.** Simple.

Picture below for demonstration purposes only:



Q16

A 14-year-old girl is brought to the physician by her mother because of a 2-month history of hair loss on her head. The mother says that her daughter has been trying to imitate the hairstyles of several pop music stars by using various ties, rubber bands, and curlers, but she is not sure whether any chemical treatments have been used. The mother reports that the patient has been sad since her grandmother died unexpectedly 3 months ago. Vital signs are normal. Physical examination shows decreased hair density over several irregular patches temporally and frontally, but no denuded areas. The underlying skin is normal. The remaining hair shafts in these thinned areas are of varying lengths. There is no frontotemporal recession. A photograph of the affected area is shown. Which of the following is the most likely explanation for this patient's hair loss?



- A. Alopecia areata
- B. Androgenetic alopecia
- C. Telogen effluvium
- D. Tinea capitis
- E. Trichotillomania

▼ Explanation

- Answer is E (Trichotillomania)

- **IMP Clues:**
 - 14y old girl
 - Ties, rubber bands, and curlers (mechanical tension of hair)
 - Grandmother died 3 months ago (psychological stress)
 - Decreased hair density over irregular patches with No denuded areas (excludes out alopecia areata, androgenic alopecia, and telogen effluvium)
 - Underlying skin normal (excludes out Tinea capitis)
 - Hair of varying lengths (establishes the dx of trichotillomania)
 - No frontotemporal recession (would normally exclude androgenic alopecia in males; in females androgenic alopecia presents as hair thinning)

- **Dx → Trichotillomania**
 - It is the **urge to pull out hair (any hair not just limited to the head) that relieves patient's stress**
 - Associated with **stressful conditions +/- other psychiatric disorders (OCD)**
 - **More common in young women**
 - Scalp Findings:
 - **Irregular patches of broken irregular hairs**
 - Scalp usually **normal** (**NO** scarring or erythema)



USMLE can give you the above vignette in a patient that then develops diffuse abdominal pain, vomiting, and distention. They then ask for diagnosis.

- Answer is **Gastric Outlet Obstruction secondary to trichobezoar** (mass of hair in intestines or stomach) **caused by Trichophagia** (ingestion of hair after pulling)

USMLE can play around in the vignettes with OCD, Trichotillomania, Trichophagia, and Trichobezoar



▼ Other Choices

Feature	Alopecia Areata	Androgenic Alopecia	Telogen Effluvium	Trichotillomania	Tinea Capitis
Etiology	Autoimmune attack on hair follicles	Genetic + androgen-mediated (DHT)	Stressor-induced premature shift to telogen phase	Psychiatric pulling of hair	Fungal infection with Tinea species
Pattern of Hair Loss	Smooth, round well-demarcated patches	Progressive thinning, frontal/vertex in men, central in women	Diffuse thinning of scalp hair	Broken hairs of varying length, bizarre/uneven pattern	Scaly patches with hair loss, possible kerion
Scalp Findings	Normal scalp	Normal scalp	Normal scalp	Normal scalp (may be inflamed if pulling was recent)	Scaling , inflammation, possible lymphadenopathy
Hair Shaft Appearance	"Exclamation point hairs" at edge of patches	Miniaturized hair follicles		Broken, irregular hairs	Broken hairs, "black dots" (hairs broken at scalp level)
Associated Conditions	Autoimmune diseases (remember, autoimmune diseases go together)	None specific	Trigger: childbirth, illness, surgery, meds	OCD, anxiety disorders	Often in children; contact with infected humans/animals
Hair Pull Test	-	-	Positive (easily extractable hairs)	-	-

Q17

A 27-year-old primigravid woman at 34 weeks' gestation is admitted to the hospital because of nausea and vomiting, and abdominal pain for 12 hours. Her pregnancy has been otherwise unremarkable. Prior laboratory studies, including a complete blood count and serologic tests for HIV and hepatitis, have shown no abnormalities. Her blood pressure now is 164/102 mm Hg. Abdominal examination shows right upper quadrant tenderness. Laboratory studies show:

Hemoglobin	7.4 g/dL
Hematocrit	24%
Platelet count	72,000/mm ³
Serum	

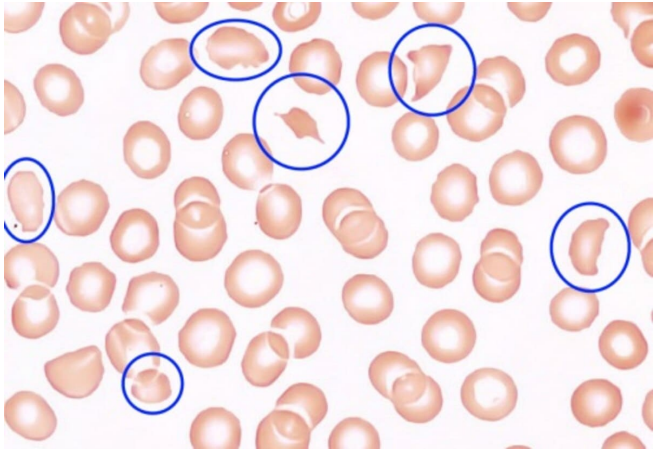
Creatinine	1.2 mg/dL
Total bilirubin	2.3 mg/dL
AST	112 U/L
ALT	126 U/L

Examination of a peripheral blood smear is most likely to show a predominance of which of the following in this patient?

- A. Acanthocytes
- B. Heinz bodies
- C. Howell-Jolly bodies
- D. Schistocytes
- E. Spherocytes
- F. Target cells

▼ Explanation

- Answer is D (Schistocytes)
 - IMP Clues:
 - Pregnant (think of all the pregnancy related disorders)
 - Negative Hepatitis & HIV serology (telling you it is not viral to help exclusion)
 - BP is 164/102 (PRE-ECLAMPSIA)
 - RUQ pain (Liver site pain?)
 - CBC: Anemia (low Hb & Hct), TCP (something destroying PLTs), elevated ALT & AST (something going on with liver)
 - Dx → HELLP Syndrome
 - HELLP stands for Hemolysis, Elevated Liver Enzymes, Low Platelets
 - Complication of **pre-eclampsia**.
 - Presents as **RUQ pain** (+/- epigastric pain) in a **late 2nd/3rd trimester pregnant female**
 - Lab evaluation reveals:
 - **Low** Platelets
 - **Increased** AST/ALT and bilirubin
 - **Increased** LDH (due to hemolysis)
 - Associated with **schistocytes** on peripheral smear:



 DD of Schistocytes on the USMLE:

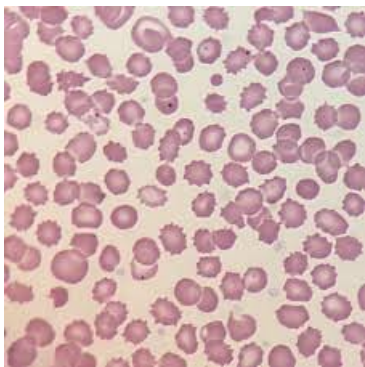
- TTP
- HUS
- DIC
- HELLP
- Mechanical hemolysis of prosthetic heart valves

? What's another name for Schistocytes the USMLE occasionally uses?

▼ Answer
Helmet Cells

▼ Other Choices

- Choice A → Acanthocytes aka **Spur cells** are cells seen usually in **Liver Failure 2ry to heat stroke**



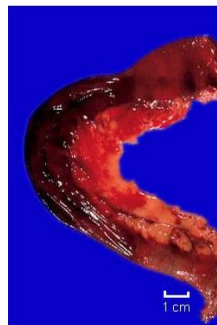
- **Choice B → Heinz Bodies** are *precipitated / oxidized hemoglobin* seen toward the periphery of the RBC in G6PD deficiency
- **Choice C → Howell-Jolly Bodies** are *nuclear remnants* a normal finding post-splenectomy

? When are Howell-Jolly Bodies seen in a patient who didn't undergo splenectomy?
 ▼ Answer
 IN SICKLE CELL PATIENTS POST AUTO-SPLENECTOMY

- **Choice E → Spherocytes** can refer to either Hereditary spherocytosis or Autoimmune hemolytic anemia
 - How to differentiate between them? **Coomb's test: HS -ve; AHA +ve**
- **Choice F → Target Cells** a finding in Thalassemia on the USMLE

Q18

While lifting weights, a 24-year-old man develops a painful swelling in the right inguinal region that cannot be reduced. The photograph shows a segment of the small intestine resected at exploratory laparotomy. Which of the following is the most likely diagnosis?



- A. Adhesions
- B. Embolism
- C. Intussusception
- D. Strangulation
- E. Volvulus

▼ Explanation

- **Answer is D (Strangulation)**
 - Easy Q here. The patient has swelling in right inguinal region (buzzy for hernia) that cannot be reduced and is painful (Complicated hernia)
 - Pic shows dark red / black intestines (ischemic / gangrenous hernia)
 - Easy diagnosis of **Strangulated Inguinal Hernia (Choice D)**

▼ Other Choices

- **Choice A → Adhesions** normally present as pain / IO with hx of some sort of GI surgery / **Caesarian section**
- **Choice B → Embolism** probably refers to Mesenteric Vascular Occlusion.
 - Risk Factors include *Estrogen, COCs, AFib, Thyrotoxicosis*
 - Usually, an adult with **SEVERE ABDOMINAL PAIN +/- Bleeding per rectum**
- **Choice C → Intussusception**
 - Almost always **under age 2**
 - Idiopathic or 2ry to Viral infection or **Rota vaccination** in which mesenteric adenitis act as a lead point for “telescoping in”, and Meckel’s Diverticulum
 - Presentation is : **intermittent/colicky abdominal pain + kid draws legs to the chest or squat + blood in the stool +/- bilious vomiting**
 - **Sausage shaped abdominal mass is what differentiates it from Midgut volvulus**
 - CT/AUS shows **Target Sign**

- **Choice E → Volvulus** on the USMLE presents in two ways:
 1. **Midgut volvulus in pediatrics:**
 - Almost always **under age 1**.
 - **Failure of rotation of proximal bowel.**
 - Presents similarly to intussusception (often mistaken for it), but there is no mass.
 - **Upper-GI series shows corkscrew appearance [ONLY MENTION IN STEP 1]**
 2. **Sigmoid volvulus in elderly:**
 - **Patient over 70 + 2-3 days of constipation + abdominal pain.**
 - Rotation around its mesentery causes "dilation of sigmoid colon"
 - Abdominal x-ray is used to diagnose, which shows a **coffee bean sign**



Volvulus Pictures:

Upper-GI series showing corkscrew appearance:

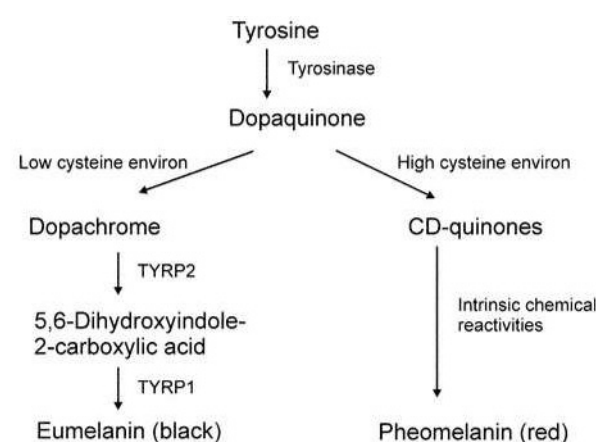


Coffee bean Sign:



Q19

A 5-year-old boy is brought to the physician for a well-child examination. He recently immigrated to the USA from Nigeria with his parents. He has no history of major medical illness. He is at the 40th percentile for height and weight. His vital signs are within normal limits. Physical examination shows red-bronze skin, red hair, and continual horizontal nystagmus. Laboratory studies show a complete blood count that is within the reference range and normal leukocyte and platelet morphology. Genetic testing shows compound heterozygosity of the TYRP1 gene in the figure shown, with the presence of both a frame-shift (368delA) and a nonsense (S166X) mutation. These genetic changes most likely caused which of the following in this patient?



- Absence of tyrosinase in the affected cells
- Decreased concentrations of 5,6-dihydroxyindole-2-carboxylic acid
- Decreased reactive oxygen species in pigmented cells
- Increased photoprotection of the prevalent melanin form
- Lack of choroidal pigment deposition in the macula

▼ Explanation

- **Answer is E (Lack of choroidal pigment deposition in the macula)**
 - Another tricky Q, let us see what we know:
 - From the stem we know that there is some sort of mutation in the TYRP1 gene so → not working & most likely tyrosine will be shunted to the other arm (to make pheomelanin).

- If a gene is not working then what it produces decreases & the substrates accumulate
 - Tyrosine is shunted into CD-quinones → intrinsic chemical reactivities (just say ROS man!) → increased pheomelanin (red)
- Okay lets eliminate to get to the answer: (using the given biochemical pathway)
- **Choice A** → tyrosine is present (Eumelanin is absent)
 - **Choice B** → if the TYRP1 is mutated, then what is before it accumulates → Increased (not decreased)
 - **Choice C** → tyrosine is shunted to the right arm so more CD-quinones so more pheomelanin which apparently causes "increased intrinsic chemical reactivities" (do not ask me why, it is what the NBME gave us)
 - **Choice D** → black pigment is much more photoprotective than red pigment (this is why red heads burn more easily than black skin)

Q20

A 19-year-old woman is brought to the emergency department 30 minutes after falling on her outstretched right hand during a gymnastics competition. Physical examination shows tenderness of the anatomical snuff-box. An x-ray of the right wrist is shown. The most likely diagnosis is fracture of which of the following carpal bones?



- A. Capitate
- B. Hamate
- C. Lunate
- D. Scaphoid
- E. Triquetrum

▼ **Explanation**

- Answer is D (Scaphoid)

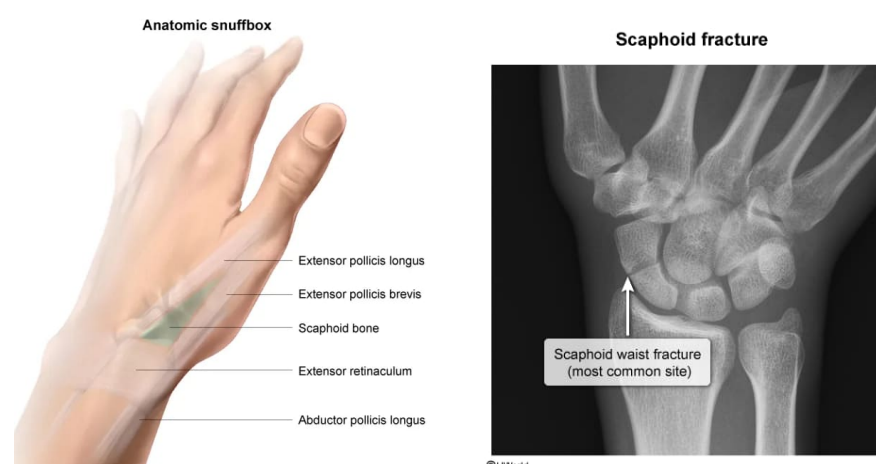
○ **IMP Clues:**

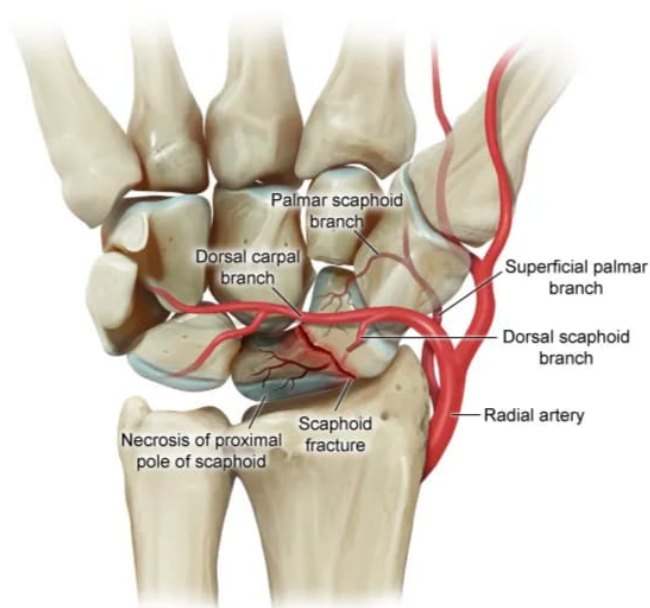
- Falling on her outstretched right hand (FOOSH fractures)
- Tenderness of the anatomical snuff-box (IMP keyword)

○ **Dx → Scaphoid Fracture**

- One of the most common fractures following **Fall on Outstretched Hand (FOOSH)**
- **Presents as wrist pain and snuff-box tenderness [on USMLE, snuff-box tenderness = Scaphoid Fracture]**
- Wrist X-ray has low sensitivity, so MRI is indicated if fracture is suspected/X-Ray is normal
 - why?
 - Due to **risk of Avascular Necrosis**, as the fracture can compromise the nearby radial artery branch

Pics below show the anatomic snuffbox (no need to know surrounding tendons) and Wrist X-Ray showing a scaphoid fracture:





Wrist X-Ray Review:



"Knowing the X-ray is important, as they can give you a presentation of either Lunate, Scaphoid, or Hamate bone injuries & ask you to choose the bone from the X-ray."

[] mnemonic: "She Looks Too Pretty, Try To Catch Her."



FOOSH with pain in central palm + **NO** pain over anatomic snuffbox is **Lunate Fracture**

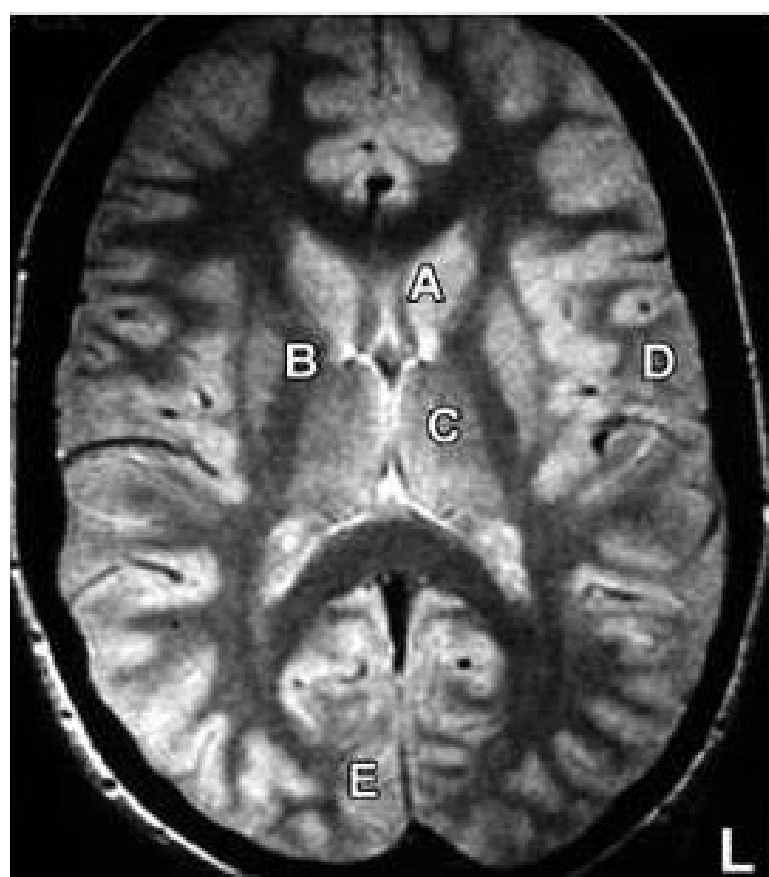
- Major complication of lunate fracture is **Carpal Tunnel Syndrome**

▼ Other Choices

- **Capitate** → never seen as an answer
- **Hamate** → causes distal ulnar nerve injury / Guyon Canal Syndrome often from handlebar injury in a bicyclist
- **Triquetrum** → Triq what?? never ever seen this is an answer, is it even a real bone?

Q21

A 66-year-old right-handed woman develops the acute onset of spastic left hemiparesis and weakness of the lower two thirds of the face on the left. The most likely cause of her condition is a lesion at which of the following labeled areas on the MRI of the brain shown?



- A. A
- B. B
- C. C
- D. D
- E. E

▼ Explanation

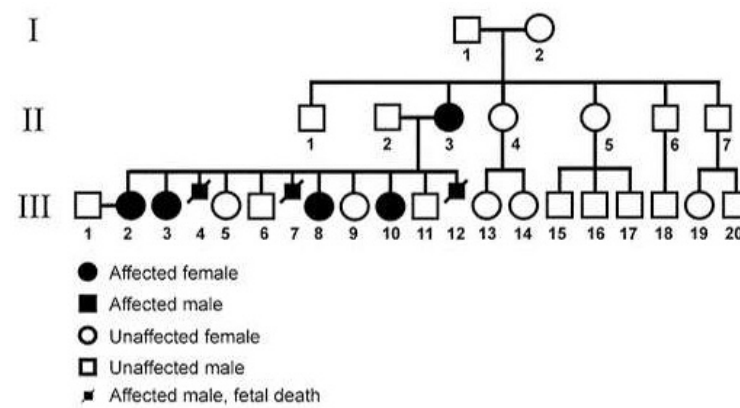
- Answer is B (Internal Capsule)
 - Just know the following: Internal capsule lesions on the USMLE cause CONTRALATERAL PURE *MOTOR* affection
 - Q says spastic paralysis so UMNL

▼ Other Choices

- Choice A → is caudate: Lesions on the USMLE cause Huntington Disease
 - AD CAG TNR expansion of chromosome 4
 - Chorea/athetosis (Irregular jerky movement of extremities & disjointed gait)
 - Neurodegeneration (Dementia)
 - Anticipation (Family Hx of similar condition & father dies earlier)
- Choice C → is Thalamus: Lesions on the USMLE cause CONTRALATERAL PURE *SENSORY* affection
 - VPL nucleus → Body
 - VPM nucleus → Face
- Choice D → is parietal lobe: irrelevant here

Q22

A 26-year-old woman (III-2) comes to the physician for counseling prior to conception. Many members of her family had blistering of the skin in infancy and now have unusual marbled pigmentation of the skin. The underlying inherited condition is uniformly fatal to males in utero. A pedigree is shown. Which of the following is the most likely risk that this patient's live-born offspring will be affected?



- A. 25% in females but near 0 in males
- B. 25% in males but near 0 in females
- C. 25% regardless of the sex of the child
- D. 50% in females but near 0 in males
- E. 50% in males but near 0 in females
- F. 50% regardless of the sex of the child
- G. Nearly 100%
- H. Not increased over the general population risk

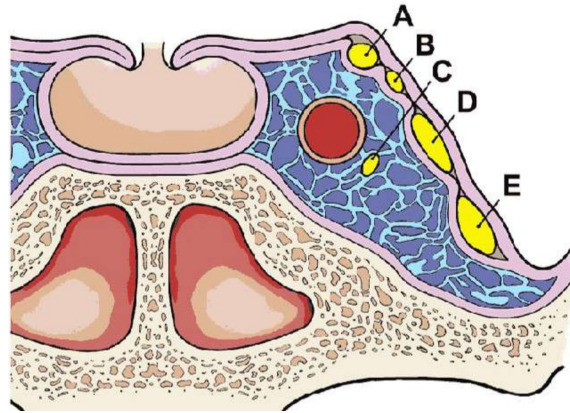
▼ Explanation

- Answer is D (50% in females but near 0 in males)
 - This Q looks hard but in fact is very easy.
 - Let's go through what we know
 - Males who get this disease die in utero
 - The pattern of this disease is **XLD**.
 - Why?
 - Always check mitochondrial transmission first → female with all her infants affected? **No**.
 - Do we have generational skip? **No**. Both the 2nd & 3rd generations are affected (1st gen is here to throw you off) → Dominant
 - Disease is transmitted from mother to males & females equally (half of them) → **XLD**

- **Chance of being affected 50%**
 - So affected males die in utero = 0
 - females are affected 50% of the time

Q23

A 65-year-old woman undergoes surgical repair of an aneurysm of the right internal carotid artery in the cavernous sinus. Three days later, physical examination shows that the right pupil is larger than the left pupil. There is also weakness with movement of the eye. A diagram of a coronal section through the middle cranial fossa, including the cavernous sinus and associated structures, is shown. Which of the following labeled nerves is most likely damaged in this patient?



- A. A
- B. B
- C. C
- D. D
- E. E

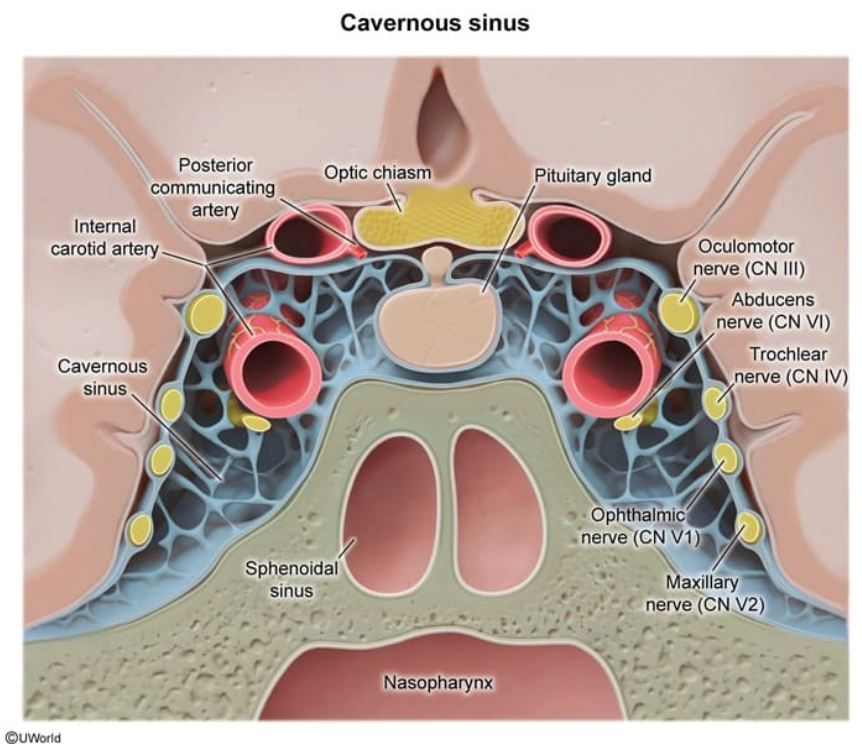
▼ **Explanation**

- **Answer is A (Oculomotor nerve)**
 - Red Circle is **Right Internal Carotid artery**.
 - An aneurysm most likely will injure the **abducens nerve (C)** as it is the closest.
 - However, the "right pupil is larger than left" meaning the **aneurysm compresses the Oculomotor nerve (A)** causing palsy.
 - Vignette also mentions weakness in movement, but this is non-specific



A good mnemonic to remember the order of the nerves on the lateral wall of the cavernous sinus is: "**OTOM**"

- **O** - Oculomotor (option A)
- **T** - Trochlear (option B)
- **O** - Ophthalmic division of trigeminal nerve (option D)
- **M** - Maxillary division of trigeminal nerve (option E)





Remember that!

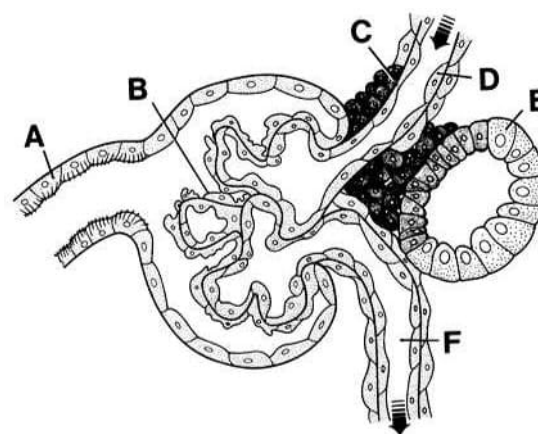
- **Abducens nerve (CN6)** causes **Abduction** of eye via control of **lateral rectus muscle**.
- **Ophthalmic division of Trigeminal n (V1)** → exits skull through **Superior orbital fissure**
- **Maxillary division of Trigeminal n (V2)** → exits skull through **foramen Rotundum**
- **Mandibular division of Trigeminal n (V3)** → exits skull through **foramen Ovale**

Mnemonic to remember the exits of the trigeminal nerve exits is: **"SRO"**

- **S** - **S**uperior orbital fissure for V1
- **R** - foramen **R**otundum for V2
- **O** - foramen **O**vale for V3

Q24

A 54-year-old man comes to the physician for a routine health maintenance examination. His pulse is 80/min, respirations are 14/min, and blood pressure is 140/95 mm Hg. Physical examination shows no other abnormalities. An angiotensin I-converting enzyme inhibitor is prescribed. Which of the following labeled regions in the illustration of the kidney shown will be most affected by the administration of this drug?



- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

▼ **Explanation**

- Answer is F (Efferent Arteriole)

- HY to know that Renal Flow is affected by 2 mechanisms:

1. **Prostaglandins**

- PGs effect on renal flow is **VASODILATION** of **afferent** arterioles

HY to know that PGs **increase** GFR & RPF → maintains FF (No Net Change)

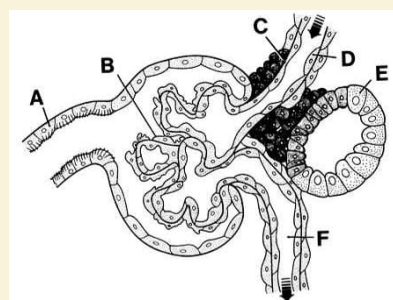
- **NSAIDs decrease PGs → DECREASE VASODILATION**

- So NSAIDs → **decrease** GFR & RPF → maintains FF (**No Net Change**)



Can worsen renal failure due to **decrease of GFR** so avoided in patients with renal insufficiency!

"USMLE will give you a picture like the above pic & asks you to where NSAIDs/PGs and ACEi/AT-II act on the nephron. So, get comfortable with it."



▼ NSAIDs/PGs act on afferent arterioles (D)

▼ AT-II act on efferent arterioles (F)

Where does ACE inhibitors act?

- **IN THE LUNGS**

- ACE is produced in the lungs

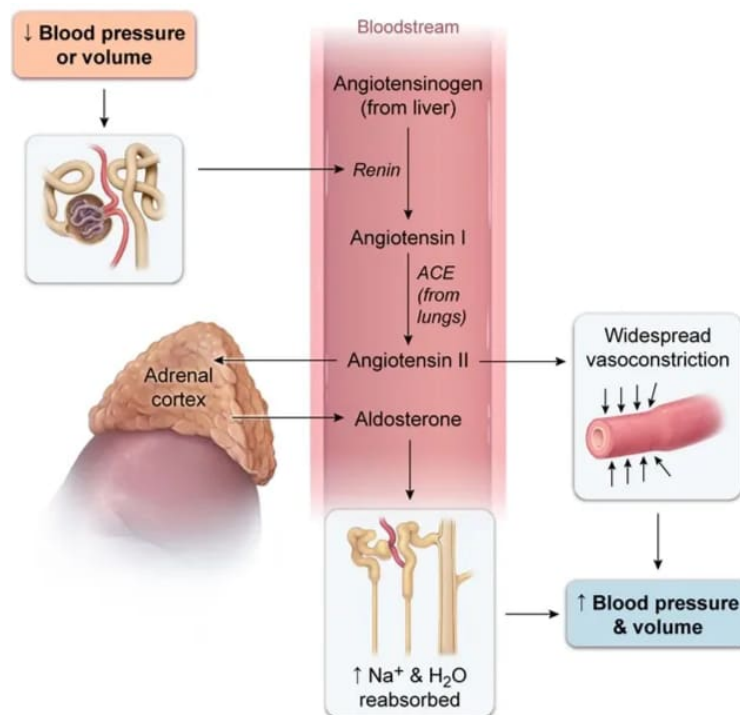
2. Angiotensin-2

- AT-II effect on renal flow is **VASOCONSTRICTION** of *efferent* arterioles

HY to know that ACE increases GFR but doesn't affect RPF → increases FF

- ARBs inhibit AT-II receptors → DECREASE VASOCONSTRICTION**
- ACE inhibitors inhibit ACE, which decreased conversion of AT-I to AT-II → DECREASE VASOCONSTRICTION**

Remember the RAAS?



Renal Physiology Rapid Review:

- Filtration Fraction = GFR/RPF; Normal = 20
- GFR can be estimated by:**
 - Inulin (**BEST**) → Freely filtered & neither secreted nor absorbed so predicts GFR exactly
 - Not used clinically
 - Creatinine → Filtered & slightly secreted in PCT so slightly overestimates GFR
 - Used clinically
- RPF can be estimated by:**
 - PAH clearance → All of it is excreted**

Q25

A study is conducted on patients with asthma to compare a new asthma treatment with a placebo. After 12 weeks of therapy, the mean ($\pm$ standard error of the mean) symptom scores were 2.8 ± 0.1 in the treated group ($n=103$) as compared to 3.1 ± 0.1 in the placebo group ($n=100$). The p-value is 0.035. The investigators of this study state that they chose a sample size of about 100 subjects in each group to have an 80% power of detecting a mean difference of 0.4 at a significance level of 5%. When planning a study, which of the following is the meaning of "80% power"?

- If 80% of the subjects improve with the drug, there is a 95% chance that a study of this size will find a p-value ≥ 0.05
- If 80% of the subjects improve with the drug, there is a 95% chance that a study of this size will find a p-value ≤ 0.05
- If the treatment decreases the asthma score by 0.4 in 80% of the subjects, there is a 95% chance that a study of this size will find a p-value ≥ 0.05
- If the treatment decreases the asthma score by 0.4 in 80% of the subjects, there is a 95% chance that a study of this size will find a p-value ≤ 0.05
- If the treatment really changes the mean asthma score by 0.4, there is an 80% chance that a study of this size will find a p-value ≥ 0.05
- If the treatment really changes the mean asthma score by 0.4, there is an 80% chance that a study of this size will find a p-value ≤ 0.05

▼ Explanation

- Answer is F**
 - First of all, go watch Dr. Osama ElSawwah Biostat playlist. IT IS THE BEST OUT THERE.
 - What is Power?** → Power is essentially the True Positive. In other words, power is the % that actually says that the hypothesis is actually true & there is a TRUE finding/relation.
 - What is P-value?** → P-value is essentially the ALPHA. In other words, ALPHA is the False Positive. In other words, again, it is the % that says that the positive results support the hypothesis when they actually DON'T. Read this one more time.
 - To be more precise, there is a slight difference between the actual meanings of p-value & alpha.
 - Alpha is the "margin of error" agreed on *BEFORE* the experiment is started.
 - P-value is the "margin of error" that was *ACTUALLY MEASURED AFTER* the experiment has ended
 - The alpha is usually set to 5%

- if p-value is equal to or less than alpha → findings are **reliable (clinically significant)**
 - if p-value is more than the alpha → findings are **NOT reliable (NOT clinically significant)**
- **So, Choice F says:** If the treatment really changes the mean asthma score by 0.4 [The Finding], there is an 80% chance [TP] that a study with size will have a p-value of less than or equal to 0.05 [margin of error]

Q26

A 52-year-old woman is admitted to the hospital because of shortness of breath due to malignant ascites and pleural effusion. She has had ovarian cancer for 3 years. Treatment has included several courses of aggressive chemotherapy including intraperitoneal chemotherapy and sclerotherapy for her recurrent pleural effusion. During prior hospitalizations, she has undergone debulking procedures. She has been discouraged by the ineffectiveness of therapy, and she feels emotionally and physically exhausted. Her primary care gynecologist suggests a palliative care consultation, but her gynecologic oncologist says he is "absolutely opposed to giving up" and is recommending referral for inclusion in a clinical trial. This disagreement between the two physicians is disconcerting to the patient. Following thoracentesis and paracentesis, the patient calls her primary care internist to help address this conflict between the two physicians. Which of the following is the most appropriate next step for the internist to address the patient's concerns?

- A. Contact a representative from the hospital risk management department
- B. Speak with the chair of the hospital ethics committee
- C. Speak with the two gynecologists to attempt to coordinate care
- D. Refer the patient for pastoral counseling
- E. Refer the patient for a psychiatric consultation to deal with her anxiety about the conflict

▼ **Explanation**

- **Answer is C (Speak with two gynecologists to attempt to coordinate care)**
 - Ethics Qs require some sort of dumbness sometimes
 - **Choice C** is correct because this is the only answer choice that would fix the problem + one of the duties of a primary care physician is to coordinate care
 - **Choices A & B** → are NEVER the correct answer on the USMLE
 - **Choice D** → is nonsense because why would she need a priest
 - **Choice E** → is also nonsense because the problem is still there (the conflict between the gynecologists)

Q27

A 65-year-old woman is being treated in the hospital for widely metastatic breast cancer unresponsive to chemotherapy. She has never married and has no children or siblings. Throughout her illness, another woman she had introduced as "my close friend," has been with her during hospitalizations and office visits. The patient is moved to an inpatient hospice after she decides she wants no further curative therapy. She and her friend appear very distressed when they read a sign outside the hospice unit that states only family members are permitted to stay after visiting hours. Her friend says, "We can't bear to be apart. It would be cruel to separate us now." Which of the following responses by the physician is most appropriate?

- A. "Don't worry. I'll call you right away if something happens to your friend. Just leave your number with the nurses."
- B. "I'm sorry, but only family is allowed to stay with patients in the hospital. You will have to leave after your 15 minutes are up."
- C. "The two of you seem to have a very important relationship. Of course you may stay together."
- D. "Visiting hours are posted outside. You are welcome during any of those times. I'm sorry, but an exception cannot be made in your case."
- E. "Well, I guess we could bend the rules just this time, but if anyone asks, you're her sister. Does that sound OK?"

▼ **Explanation**

- **Answer is C ("The two of you seem to have a very important relationship. Of course you may stay together.")**
 - Another ethics Q, let us see what to do:
 - The patient has no children & siblings but has a "close friend" (when ever this happens on the USMLE, be nice to the close friend)
 - **Choice A** → is a good choice but this would cause distress & anxiety for both the friend & the patient
 - **Choices B & D** → are just rude & would also cause distress & anxiety for both of them

- **Choice E** → NEVER LIE. NEVER.

Q28

A 34-year-old woman comes to the physician because she has been feeling weepy and overwhelmed since delivering a healthy male newborn 6 weeks ago. She has had fatigue and irritability during this period, and she has had no interest in engaging in activities she used to enjoy prior to the birth of the baby. She also has had difficulty sleeping because she is always listening for sounds indicating that her baby is awake. She says, "My husband doesn't help me at all with the baby. We argue all the time now." She then says, "I feel guilty because I'm not enjoying my baby more. I don't know if I will be a good mother or not." Physical examination shows no abnormalities. Which of the following statements by the physician is most appropriate?

- A. "Has it come as a surprise to you how hard parenting is? Many people feel that way."
- B. "I'm concerned about how bad you've been feeling lately. Have you had any thoughts about death or wanting to be dead?"
- C. "I'm sure that you'll feel better soon. After all, look at your beautiful baby."
- D. "Most new mothers feel this way, and sometimes it helps to see a therapist. Would you like me to give you a referral?"
- E. "Your relationship with your husband sounds strained. I don't blame you for being angry with him."

▼ **Explanation**

- **Answer is B**
 - Yet another ethics Q (get used to it). We have a patient with major Depressive Disorder
 - **VERY HY TO KNOW → In patients with depression, it is VERY IMP to screen for suicidal ideation or harming other people.**
 - MDD with peripartum onset lasts > 2 weeks
 - Postpartum baby blues last for < 10 days
 - Post-partum psychosis involves thoughts of harming the baby or self

▼ **Other Choices**

- **Choices A & C** → disregards her distress
- **Choice D** → is a good choice, but you need to screen for thoughts of self-harm or harming of other first.
- **Choice E** → is nonsense.

Q29

A 75-year-old man with dementia, Alzheimer type, is brought to the hospital by his wife because of cough, difficulty breathing, and agitation that began after he ate breakfast 2 hours ago. He has been a resident of a skilled nursing care facility for 7 years. His wife visits the facility daily to feed him his midday meals. His two adult children visit him several times weekly. His wife mentions that the patient has been coughing during his meals for several weeks. He also has been taking longer to finish even smaller portions of food. Results of imaging studies are consistent with aspiration pneumonia with a developing compromised swallowing function. His medical records show no advance directives. In speaking with the patient's family, it is most appropriate for the physician to address the issue of a feeding tube in which of the following manners?

- A. Encourage the family to come to a consensus based on their perception of the patient's wishes
- B. Explain that a feeding tube is difficult to monitor and may not prevent aspiration
- C. Follow only the wishes of the wife
- D. Help the adult children encourage the wife to start a gradual withdrawal from the patient
- E. Recommend a tube, because feeding will be more efficient and prevent starvation

▼ **Explanation**

- **Answer is A (encourage the family to come to a consensus based on their perception of the patient's wishes)**
 - How many ethics Q in a row?? Let us see what we have here.
 - **Two very IMP concepts here:**
 1. The patient (or their family, if they lack decision-making capabilities) is the one who makes their decision. All you do as a physician is present them with all the options & details
 2. The decision-making hierarchy on the USMLE: **wife/husband → children → parents → siblings.**
 - So, **the best answer here** is to encourage the family to reach an agreement based on what the patient would have wanted (**Choice A**)

▼ Other Choices

- **Choice B** → is medically incorrect
- **Choice C** → would be correct according to the decision making hierarchy if the family could NOT reach an agreement
- **Choice D** → is just a straight no.
- **Choice E** → is medically correct, but remember that it is the patient's (or his family if he lacks decision making capabilities) decision. Not yours.

Q30

A 25-year-old woman has a 3-week history of bleeding gums while brushing her teeth and easy bruising. She appears anxious but alert. There is no lymphadenopathy or organomegaly. Irregular bruises are noted on her legs, thighs, and arms. Numerous petechiae are noted on the left arm distal to where the blood pressure cuff is used. She delivered a healthy child 9 months ago and is not taking any medications except for an oral contraceptive. Laboratory studies show:

Hemoglobin	12.5 g/dL
Mean corpuscular volume	80 μm^3
Leukocyte count	8500/mm ³
Differential	normal
Erythrocyte morphology	normal
Platelets	rare but large
Platelet count	18,500/mm ³
Urinalysis	unremarkable

Which of the following is the most likely cause of her condition?

- A. Acquired antibodies against platelet antigen P1A1
- B. Autoantibodies against platelet glycoproteins
- C. Folic acid deficiency
- D. Viral suppression of marrow megakaryocytes
- E. Widespread damage to endothelial cells

▼ Explanation

- **Answer is B (Autoantibodies against platelet glycoproteins)**
 - **IMP Clues:**
 - Bleeding gums, easy bruising, petechiae (most likely a PLT disorder)
 - No lymphadenopathy or Organomegaly (excludes some etiologies like Leukemia)
 - Nonsignificant drug history (not drug induced) [COCs should cause INCREASED Clotting]
 - Hx of delivering a baby (could be relevant as ITP is triggered by pregnancy)
 - LOWWW PLT count (normal 150,000-450,000)
 - **Dx → ITP**
 - Antibodies against **Glycoproteins 2b/3a on PLTs (Type 2 Hypersensitivity)**
 - **GP 2b/3a** are responsible for PLT **aggregation**
 - **GP 1b** is responsible for PLT **adhesion**
 - **Destroyed PLTs → Decreased PLT count - Increased Bleeding Time - No Change in PT or PTT**
 - Precipitated by **Viral infections - post-pregnancy - or even idiopathically**
 - "Most vignettes on the USMLE will be either a female with random bruising and low PLTs or increased BT and no / subtle risk factors present OR a child who had a cough / cold then developed petechia or bruises or epistaxis (some kind of bleeding)"

▼ Other Choices

- **Choice A** → refers to Neonatal Alloimmune TCP (not assessed on STEP 1 I think)- just know that maternal antibodies attack PLTs of her fetus (woman not affected here, the baby is)
- **Choice C** → would have high MCV (100+)

- **Choice D** → would most likely cause pancytopenia not isolated TCP + no history of infection mentioned
- **Choice E** → can refer to either TTP or HUS or DIC:
 - **HUS**
 - Hx of **bloody diarrhea** (most likely **Shiga toxin or Shiga-like toxin of EHEC**)
 - Presents as **Triad of** → **TCP + Hemolytic anemia with Schistocytes + Renal Failure +/- hematuria**
 - Mechanism: Toxins cause inflammation of renal microvasculature → **ADAMTS13 protein** inactivation → failure of cleavage of vWF multimers → platelet adherence to vascular endothelium cannot be as readily reversed → platelet aggregations protrude into vascular lumen causing shearing of RBCs flying past → fragmentation of RBCs (schistocytes, aka helmet cells)
 - **TTP**
 - Hx of **viral infection / no hx given**
 - Presents as a **pentad of** → **HUS + fever + stroke-like/neurological findings**
 - Mechanism: caused by antibodies against, or a mutation in, **ADAMTS13** → failure of cleavage of vWF multimers → platelet adherence to vascular endothelium cannot be as readily reversed → platelet aggregations protrude into vascular lumen causing shearing of RBCs flying past → fragmentation of RBCs (schistocytes, aka helmet cells)

? What is ADAMTS13?

▼ **Answer**

ADAMTS13 is a metalloproteinase that breaks down von Willebrand factor multimers

Q31

A 34-year-old woman is brought to the emergency department 30 minutes after she fell unconscious on a downtown sidewalk of apparent alcohol intoxication. At the scene, her companion tells the emergency medical technicians that the patient regularly ingests alcoholic beverages but "can usually hold her liquor better." On arrival, she is intubated. Physical examination shows no other abnormalities except for mild cyanosis. Laboratory studies show:

Serum	
Na+	140 mEq/L
K+	5.3 mEq/L
Cl-	105 mEq/L
HCO3-	10 mEq/L
Arterial blood gas analysis on room air:	
pH	7.25
Pco2	23 mm Hg
Po2	78 mm Hg

Which of the following is the most likely interpretation of the arterial blood gas findings in this patient?

- A. Mixed respiratory acidosis and metabolic acidosis
- B. Primary metabolic acidosis with increased anion gap
- C. Primary metabolic acidosis with normal anion gap
- D. Primary respiratory acidosis with increased anion gap
- E. Primary respiratory acidosis with normal anion gap

▼ **Explanation**

- **Answer is B (Primary metabolic acidosis with increased anion gap)**
 - **IMP Clues:**
 - **Anion gap = Na - (Cl + HCO3)**
 - high gap is 13 or greater (**12 is normal & asked on NBME**)
 - Here anion gap is $140 - (105 + 10) = 140 - 115 = 25 \text{ mEq/L} =$
High Anion Gap Metabolic Acidosis
 - pH = 7.25 (normal 7.35-7.45) = **Acidosis**
 - HCO3 = 10 (normal is 22-28) = **Metabolic**
 - PCO2 = 23 (normal is 33-45) = **Respiratory Compensation**
 - **So, the answer is Primary metabolic acidosis with increased anion gap (Choice B)**



Causes of high anion gap: "MUDPILES"

- **M = Methanol**
- **U = Uremia** (Renal Failure acute or chronic)
- **D = DKA**
- **P = Phenformin** (NON-EXISTANT ON THE USMLE)
- **I = Iron (HY) or Isoniazid (HY)**
- **L = Lactic acidosis**
- **E = Ethylene glycol**
- **S = Salicylates** (Aspirin)

- There is also **respiratory compensation**



HY causes of *normal* anion gap metabolic acidosis on the USMLE:

- RTA
- Diarrhea

Q32

A healthy 8-year-old boy is brought to the physician by his parents because of a long history of disruptive behavior at school and poor academic performance. During class, he talks out of turn, wanders around the room, and pesters classmates. He is easily distracted and cannot keep his attention on a topic very long. His homework is sloppy and usually incomplete; he often explains that he leaves segments of assignments undone because he "just didn't notice them." He has had similar problems since kindergarten. He has normal developmental milestones. He is bright and cheerful and has a caring family. A drug with which of the following actions is most likely to be useful for this patient?

- A. Stimulation of the release of excitatory amino acid neurotransmitters
- B. Blockade of postsynaptic excitatory amino acid neurotransmitter receptors
- C. Stimulation of the release of biogenic amine neurotransmitters
- D. Blockade of postsynaptic biogenic amine neurotransmitter receptors
- E. Stimulation of the release of inhibitory amino acid neurotransmitters
- F. Blockade of postsynaptic inhibitory amino acid neurotransmitter receptors

▼ **Explanation**

- **Answer is C (stimulation of the release of biogenic amine neurotransmitters)**

- **IMP Clues:**

- Easily distracted + short attention span + poor academic performance (screaming ADHD)
- Similar problems since kindergarten (present since birth so not an adverse effect of something like “sniffing glue”)
- Normal developmental milestones (so not neurological related)

- **Dx → ADHD**

- Pathophysiology → **Deficient catecholamines (Dopamine & Norepinephrine) signaling**
- Treatment may be *stimulant* meds or *non-stimulant* meds

- **Most common ttt is *Methylphenidate* or *Amphetamines***

- **Methylphenidate:** Block norepinephrine and dopamine reuptake at synapses in the prefrontal cortex.
- **Amphetamines:** Block norepinephrine and dopamine reuptake at synapses in the prefrontal cortex, increase the release of norepinephrine & dopamine from presynaptic storage vesicles, and inhibit monoamine oxidase.
- So, basically they **increase catecholamines (especially Dopamine & Norepinephrine) in synaptic cleft, overcoming the deficient catecholamine signaling.**

Pharmacotherapy for attention deficit hyperactivity disorder		
Category	Medication	Adverse effects
Stimulant	Methylphenidate	Weight loss, decreased appetite, insomnia, abdominal pain, tachycardia, hypertension, tics (rare), addiction potential
	Amphetamine salts	
Nonstimulant	Clonidine	Sedation, dry mouth, constipation, irritability, anxiety, hypotension, abdominal pain, sleep disturbances (eg, nightmares)
	Guanfacine	
	Atomoxetine	Dry mouth, decreased appetite, insomnia, hyperhidrosis, erectile dysfunction



***Biogenic amines* refer to amines that were formed by decarboxylation.**

▼ **Other Choices**

- **Choices A & B** → Excitatory amino acids refer to Glutamate & Aspartate. No role here
- **Choices E & F** → Inhibitory amino acids refer to GABA & Glycine. No role here.
- **Choice D** → Hypothetically speaking, if you were to give a drug that would block the receptors of dopamine & norepinephrine (the deficient amines in ADHD), this would worsen the condition. Not Good.

Q33

A 61-year-old woman is brought to the physician by her 62-year-old husband because of a 9-month history of increasing forgetfulness. Her husband says, "I'm worried because she forgets about dinner on the stove and it ends up burned. Once she even left the bathtub running, and it overflowed and flooded the bathroom." He adds that she had always been a meticulous gardener, but now the flowerbeds have become uneven, with some areas flourishing and others seemingly untouched. Physical examination shows no abnormalities. During the mental status examination, the patient is pleasant and cooperative. She describes her mood as good. She admits to being forgetful and feels badly about upsetting her husband and burning the food so often. Her Mini-Mental State Examination score is 22/30. Which of the following is the most appropriate pharmacotherapy?

- A. Donepezil
- B. Fluoxetine
- C. Imipramine
- D. Melatonin
- E. Risperidone
- F. Vitamin B1 (thiamine)
- G. Vitamin E

▼ Explanation

- Answer is A (Donepezil)

- IMP Clues:

- 9 months hx of forgetfulness & change of gardening habits (gradual onset cognitive decline)
 - Physical Examination unremarkable (if motor / sensory affection then NOT Alzheimer)
 - MMSE score of 22/30 (Dementia is low 20s - Benign Aging is usually 28+)

- Dx → Alzheimer Dementia

- Gradual-onset **cognitive decline**, **progressive memory loss**, and **disorientation** with **low MMSE score (low 20s)**

- **NO** Sensory or Motor affection

! Dementia + sensory/motor affection → **Vascular Dementia**

- Pathophysiology: accumulation of **Beta-amyloid plaques** & **Neurofibrillary tangles** ⇒ **Neuronal loss** & **Cortical Atrophy**, which causes:

- **Widening of the sulci and narrowing of the gyri**
 - **"apparent" ventriculomegaly 2ry to cortical atrophy** ⇒ **Hydrocephalus Ex Vacuo** [asked on NBME]
 - **Atrophy of the hippocampus** ⇒ **Memory Loss**
 - **Neuronal loss** ⇒ **decreased ACh** (this is why ttt is **AChE inhibitors** → **increases ACh**)
 - Neuronal loss/death causes **release of glutamate**, which **activates NMDA receptors**
 - NMDA causes excessive Calcium influx into neurons, causing **Excitotoxicity**
 - This is also why ttt is **NMDA antagonists**, to decrease excitotoxicity & slow disease progression

- Biopsy shows → **extracellular Beta-amyloid plaques** & **intracellular Neurofibrillary tangles** (hyperphosphorylated tau proteins)

! **Frontotemporal dementia (Pick Disease)** also has **accumulation of hyperphosphorylated tau proteins** but in **round silver staining inclusion bodies**, named **Pick Bodies**.

- Genetics:

- **Down Syndrome** is associated with Early onset Alzheimer due to the presence of **"Amyloid Precursor Protein"** gene on **chromosome 21**, they have 3 chromosomes 21s, so higher chance.
 - **Presenilin Gene** mutations also cause Alzheimer.
 - **Presenilin-1/2** (on chromosomes 14/1, respectively) is a *protein that cleaves Amyloid* → if mutated → amyloid **accumulates**
 - **ApoE ε4** ⇒ **Late-Onset Alzheimer Disease**; however, **ApoE ε2** ⇒ **Protective from Alzheimer Disease**.

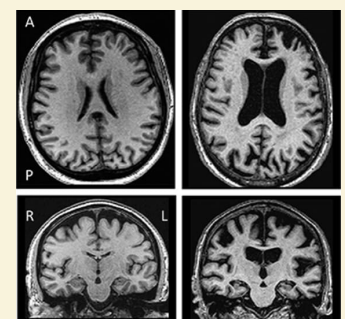
📌 Underrated HY Alzheimer Disease Complications:

1. **Amyloid Angiopathy** in brain parenchyma → **ICH**
2. **Infections** (most notably **UTIs** on the USMLE) cause worsening of dementia → **Delirium**

Sundowning is worsening of dementia at night that can resemble delirium

- ttt is decreasing ambient noise & distraction.

📷 Normal vs AD patient Brain MRI:



- Treatment: **AChE inhibitors** (Donepezil - Galantamine - Rivastigmine) or **Memantine** (NMDA glutamate antagonist)

Q34

A 45-year-old woman is brought to the emergency department 45 minutes after she was involved in a motor vehicle collision. Her temperature is 37.4°C (99.3°F), pulse is 100/min, respirations are 28/min and shallow, and blood pressure is 105/74 mm Hg. Physical examination shows numerous lower extremity lacerations. There are multiple fractures that require deep sedation before treatment because of pain. She is intubated with a cuffed endotracheal tube and mechanically ventilated with supplemental oxygen (FIO₂=1.0). The patient's ventilator settings are adjusted to deliver a tidal volume of 400 mL and 18 breaths/min, and a positive end-expiratory pressure (PEEP) of 10 cm H₂O is applied. Application of PEEP will most likely prevent which of the following complications in this patient?

- A. Absorption atelectasis
- B. Cardiogenic edema
- C. Pleural effusion
- D. Pulmonary hypertension
- E. Tension pneumothorax
- F. Tracheal dissection

▼ Explanation

• Answer is A (Absorption Atelectasis)

- **What is PEEP?** → Positive End-Expiratory Pressure is a setting on the ventilator that keeps a little bit of air (pressure) within the lungs at the end of expiration
 - **Function** → **to prevent the alveoli from collapsing (atelectasis) & to improve oxygenation**
- **Used in patients with ARDS, shallow breathing (usually trauma patients), or high FiO₂**
 - **ARDS** → presence of **protein-rich fluid in alveoli disrupts surfactant** → **alveoli collapse easily**
 - Additionally, patients with ARDS usually have **higher RR** (so shallow breathing)
 - **Shallow breathing** → **alveoli do not fully expand** so air doesn't reach them well
 - little amount of stagnant air trapped in them → **air is absorbed & the alveoli collapses**
 - **High FiO₂** → causes nitrogen washout (normally helps keep alveoli open) so collapses
 - FiO₂ = Fraction of Inspired Oxygen (% of O₂ in air breathed in)
 - FiO₂ in normal atmospheric air is 0.21 (Oxygen makes 21% of atmospheric air)
- **Risks of using PEEP:** (I have seen assessed on the USMLE include)
 - **Barotrauma (pneumothorax)** → excess pressure causing alveoli to rupture
 - **Low CO / hypotension** → increased intrathoracic pressure → decreased venous return (preload) → decreased CO

▼ Other Choices

- **Choice B** → PEEP can be a **treatment** (not a prevention) to cardiogenic edema (pulmonary edema 2ry to cardiogenic shock) by decreasing preload (remember, increased intrathoracic pressure → decreased VR → decreased preload)
- **Choice C** → Irrelevant; pleural effusion is caused by increased vascular / lymphatic permeability
- **Choice D** → PEEP actually can worsen pulmonary HTN by increasing alveolar pressure → compresses pulmonary capillaries around it → increased pulmonary vascular resistance → worsening of pulmonary HTN
- **Choice E** → Tension pneumothorax is a complication of PEEP



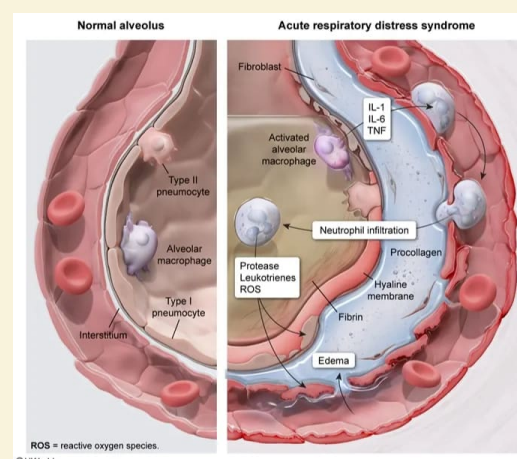
ARDS Rapid Review:

Pathophysiology: Injury to alveoli & endothelium = inflammation = increased vascular permeability = **protein-rich fluid leakage into alveoli [hyaline membranes = fibrin + necrosis]** = gas exchange impairment.

Causes:

(commonly seen on NBMEs)

- Sepsis
- Pneumonia
- Pancreatitis
- Aspiration (of gastric contents)
- Drowning
- Transfusion reactions



HY Random Facts: **[asked on NBME]**

- **Surface Protein D** is a lung injury marker that **INCREASES** in people **with ARDS** or **RECOVERING from ARDS**.
- ARDS causes **restrictive lung disease pattern**.
- ARDS is a cause of **increased A-a gradient hypoxia**.
- **Type 2 pneumocytes** regenerate the necrotic endothelium.

- **Choice F** → Irrelevant; may be a complication of mechanical intubation

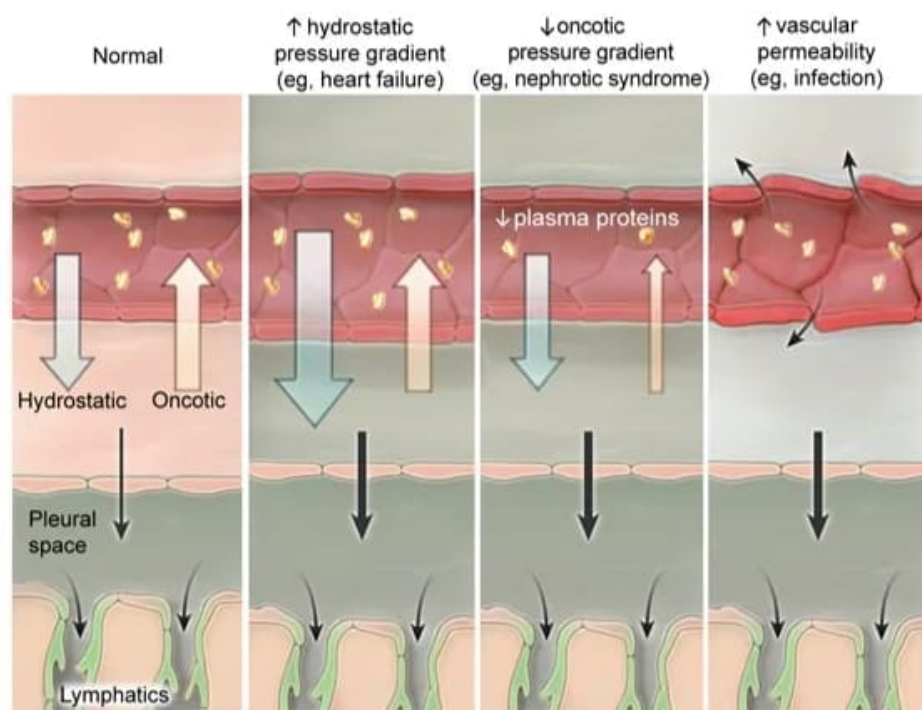
Q35

An investigator is studying the regulation of pulmonary lymphatic flow using an animal model. Catheters are implanted in the femoral vein, pulmonary artery, and main lymphatic vessel draining the lungs in anesthetized, intubated, mechanically ventilated animals. Drugs may be injected directly into the pulmonary artery catheter and inspired gas mixtures altered at the ventilator; timed collection of lymph from the catheters is used to calculate lymphatic flow. Which of the following interventions will most likely increase the flow of pulmonary lymph in these animals?

- A. Administration of endothelin-1 into the pulmonary artery
- B. Administration of phenylephrine into the pulmonary artery
- C. Decreasing the inspired oxygen concentration from 21% to 10%
- D. Increasing the inspired carbon dioxide concentration from 0.3% to 3%
- E. Intravenous infusion of 0.9% saline for 5 minutes
- F. Intravenous infusion of 20% albumin solution (20 g/100 mL saline) for 5 minutes

▼ Explanation

- **Answer is E (IV infusion of 0.9% saline for 5 mins)**
 - Q asks what will increase flow of pulmonary lymph (this is another way of saying "What will cause increase pulmonary hydrostatic pressure?")
 - **IV infusion of saline would increase amount of fluid in vessel → Increased capillary hydrostatic pressure → Extravasation of fluid into interstitial space → Lymphatic vessels drain excess interstitial fluid → Increased Lymph Flow**



▼ Other Choices

- **Choice A** → would cause less fluid in vessel → less capillary hydrostatic pressure
 - Endothelin is a potent vasoconstrictor **(NOT JUST LIMITED TO THE LUNGS) [asked on NBME]**
 - Primary Pulmonary HTN is a disease caused by a BMPR2 gene mutation
 - USMLE likes Endothelin-1 **INCREASED** in these patients
 - Presents on the USMLE as a second/third decade woman, non-smoker, with increased pulmonary vascularity/markings and either a loud P2 or tricuspid regurgitation

? What is a HY drug that relates to Endothelin?

▼ Answer

Bosentan is an Endothelin-1 receptor antagonist used for Pulmonary HTN

- **Choice B** → would also cause less fluid in vessel → less capillary hydrostatic pressure
 - Phenylephrine is an alpha 1 agonist used mainly for nasal congestion (causes VC so decreased congestion)

- **HY to know that it (and other alpha 1 agonists: Oxymetazoline & Midodrine) cause rhinitis medicamentosa → after about 3 days of usage, its effect decreases & can cause rebound nasal congestion when stopped**
- **Choices C & D** → would cause less fluid in vessel → less capillary hydrostatic pressure
 - **HY to know: Hypoxia causes VD all around the body EXCEPT IN THE LUNGS.**
 - Hypoxic VC is a HY phenomena in which the lungs react to hypoxic areas by VC → Blood **SHUNTS** away to other well ventilated area → this causes decreased V/Q ratio
 - Almost all lung conditions on the USMLE involve shunting, EXCEPT → Pulmonary Edema
 - In Pulmonary Edema, Perfusion is decreased (Embolus in Pulmonary Artery), but ventilation is intact → This area is referred to as “Dead space” → this cause increased V/Q ratio
- **Choice E** → would increase the oncotic pressure → this would cause fluid to actually move into the lung from the interstitial.

Q36

A 55-year-old woman comes to the physician because of a 6-month history of bone pain. She has a 20-year history of type 2 diabetes mellitus and has been receiving hemodialysis for the past 5 years. She cannot recall which medications she is taking, but she admits that she often forgets to take all of them. Physical examination shows no abnormalities. Serum studies show:

Ca ²⁺	8.2 mg/dL
Creatinine	9.5 mg/dL
Phosphorus	8 mg/dL
Alkaline phosphatase	180 U/L

This patient's bone pain is most likely caused by which of the following changes in serum concentrations?

- Decreased 25-hydroxycholecalciferol
- Decreased parathyroid hormone
- Decreased parathyroid hormone-related protein
- Increased 25-hydroxycholecalciferol
- Increased parathyroid hormone
- Increased parathyroid hormone-related protein

▼ Explanation

- **Answer is E (Increased Parathyroid Hormone)**
 - **IMP Clues:**
 - Bone Pain + Hx of hemodialysis (Renal Failure causing bone pain 'Osteodystrophy')
 - Low Ca, Increased phosphorus (this would cause high PTH)
 - High ALP (reflects increased osteoblast activities)

• **Dx → Renal Osteodystrophy causing secondary hyperparathyroidism**

- Patient has **End-Stage Kidney Failure** → Kidney cannot do what it does normally
 - Can not *reabsorb* Calcium → **Hypocalcemia**
 - Can not *secrete* Phosphorus → **Hyperphosphatemia**
 - Can not *synthesize* 1,25-OH-Vitamin D → **decreased Calcitriol**

 **Low** Calcium & **High** Phosphate levels cause **PTH to rise** → PTH wants to reabsorb Calcium & secrete phosphorus, but the kidney can't.



Osteoblast activity is reflected by ALP levels!

*“USMLE will give you a garbage bluff 10-liner Q of a disease you never heard of, and they throw in **low ALP levels**. They then ask for affected cell → **Osteoblasts**.”*



IL-1 (Osteoclast-activating Factor) inhibits Osteoprotegerin.

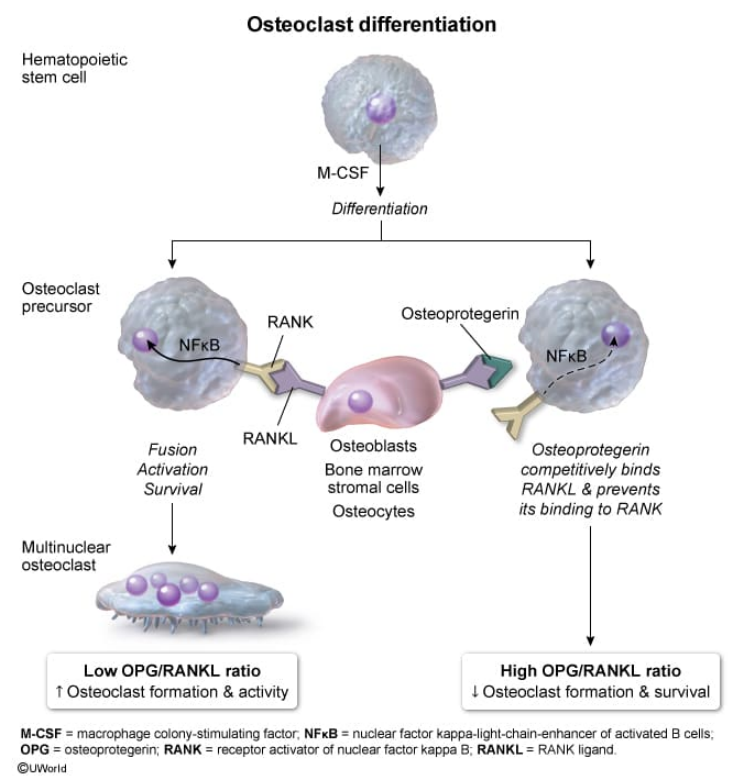
- High PTH levels **stimulate osteoblast activity** → Express **RANK-L** → binds to osteoclasts RANK Receptor → **Increase resorption of bone to increase Ca levels.**
 - **Increased bone resorption with defective bone mineralization** (replaced with fibrosis) causes **Osteitis Fibrosa Cystica** (Brown Tumor) that is characterized by **subperiosteal bone resorption, marrow fibrosis, and cystic bone lesions.**

- Presents as **bone pain, fractures, skeletal deformities, and weakness.**

USMLE might ask for the mechanism on PTH activity on osteoblasts/osteoblasts. They either ask about the highlighted description, or use "*paracrine stimulation of osteoclasts by osteoblasts,*" or "*increased osteoclasts maturation and activity*"

? What are the sites of calcium reabsorption and phosphate secretion in the kidney?

- ▼ **Answer**
Secretion of Phosphate ⇒ **Proximal** Convoluted Tubules
Reabsorption of Calcium ⇒ **Distal** Convoluted Tubules



Estrogen inhibits IL-1 (Osteoclast-activating Factor), which causes an increase Osteoprotegerin.

- This is why Estrogen causes increased bone healthy.
- Menopause = decreased Estrogen = increased IL-1 = decreases osteoprotegerin = Low OPG/RANK-L ratio = increased osteoclast activity

▼ Other Choices

- Choice A & D → Increased / Decreased 25-OH-VitD would not cause bone pain
- Choices C & F → PTH related peptide is a molecule secreted by 2 tumors on the USMLE:
 - **RCC & SCC of the lung:**
 - **ARROWS Q SO HY** → HIGH Ca - LOW Phosphate - LOW PTH
 - PTHrP is **NOT THE SAME AS PTH**. Yes it affects the labs the same as PTH, but PTH will be decreased.

Q37

A 35-year-old man is brought to the emergency department because of a 2-hour history of severe fatigue and dizziness. He has had profuse, watery diarrhea for 8 hours despite a lack of oral intake. He recently returned from a medical relief trip to a remote village in Honduras. His temperature is 36.7°C (98°F), pulse is 122/min, and blood pressure is 90/50 mm Hg. Physical examination shows dry skin and decreased capillary refill. Test of the stool for occult blood is negative; the stool is gray and turbid. A Gram stain of the stool shows predominant gram-negative, comma-shaped bacteria; there are no erythrocytes or leukocytes. Which of the following best describes the mechanism of the toxin that caused these findings?

- Activation of adenylyl cyclase
- Activation of guanylyl cyclase
- Activation of Na⁺-K⁺ATPase
- Activation of phosphodiesterase
- Deactivation of ADP-ribosylation factors

▼ Explanation

- **Answer is A (Activation of adenylyl cyclase)**
 - **IMP Clue:**
 - Profuse watery diarrhea for 8hr despite lack of oral intake (secretory diarrhea - a type of diarrhea that doesn't stop with fasting VS osmotic diarrhea that stops with fasting)
 - Hx of travel (so some kind of infection)
 - High pulse & Low BP (usually hypovolemic shock 2ry to the diarrhea)
 - Dry skin & capillary refill time (severe dehydration)

- Grey and turbid stool (trying to convey the idea of rice water stool)
 - Gram shows gram -ve, comma shaped bacteria (V.cholerae)
 - No Erythrocytes & Leukocytes (Non-invasive diarrhea)
- **Dx → Cholera**
- **Caused by *Vibrio Cholerae***
 - **Comma-shaped, Oxidase-positive, highly-motile, gram-negative rod** that is transmitted via **fecal-oral route and contaminated water**.
 - **ACID-LABILE** (so *increased risk* in patients on *PPIs*, or *with achlorhydria*)
 - Once in the intestines, **it attaches (NO invasion**, hence no erythrocytes & leukocytes in stool) & **releases Cholera Toxin**
 - ***Cholera Toxin* activates adenylate cyclase & increases cAMP**, causing excessive chloride secretion and decreased sodium reabsorption ⇒ **PROFUSE WATERY DIARRHEA**
 - USMLE likes the buzzy *"Rice Water Stools,"* or *"Grey and Turbid Stools."*



Q38

A 74-year-old woman with mild dementia is admitted to the hospital because of congestive heart failure and angina pectoris that has progressed despite maximal medical therapy. She has had three myocardial infarctions during the past 3 years. The physician recommends coronary angiography and angioplasty. The patient states that she wants to go home and does not want any medical procedures. On questioning, the patient does not know the date, the name of the hospital, or the name of her nurse who had just introduced himself. It would be most appropriate for the physician to question this patient's capacity to make a decision regarding her medical care if mental status examination showed which of the following findings?

- A. Disorientation to place and time
- B. Inability to do serial sevens
- C. Inability to recall three objects after 5 minutes
- D. Inability to understand the severity and prognosis of her medical condition
- E. Presence of depressed mood

▼ **Explanation**

- **Answer is D (inability to understand the severity and prognosis of her medical condition)**
 - For a patient to be deemed to have full capacity, he/she should have the following: **(So HY)**
 1. Understands the relevant information (understands her condition, what is the treatment, and its risks / benefits)
 2. Understands the consequences of her decision
 3. Can reason & weigh the options logically (risks & benefits)
 4. Can communicate a clear & consistent choice.

Q39

A 3-year-old boy who recently immigrated to the USA is brought to the physician by his parents because of skeletal deformities and failure to thrive. He has had listlessness, irritability, and muscle weakness most of his life. Physical examination shows frontal bossing and flattening of the back of the skull, and defects in the enamel of the teeth. The chest wall has a groove that extends from the xiphoid process transversely toward the axillae, with flaring of the rib cage below the groove. The sternal ends of the ribs bulge at their costochondral junctions. The legs are bowed. Serum calcium and phosphorus concentrations are below the reference range. If the bone were examined, which of the following findings would be most likely?

- A. Absence of cartilage in the epiphyseal plates
- B. Absence of osteoblasts
- C. Enlarged osteoclasts with increased numbers of nuclei
- D. Increased proportions of osteoid
- E. Osteosarcoma

▼ Explanation

• Answer is D (Increased Proportions of Osteoid)

◦ IMP Clues:

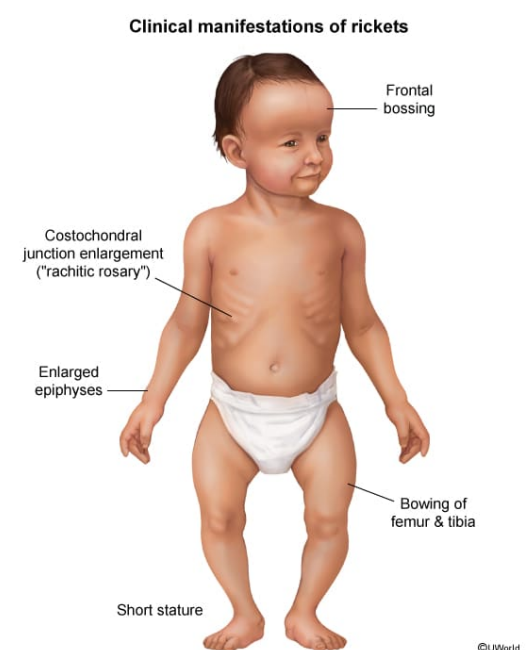
- Skeletal Deformities & Frontal Bossing
- Flattened back of skull
- Muscle Weakness
- Defects in teeth enamel
- Chest groove (Pectus excavatum)
- Subcostal groove (Harrison's grooves)
- Sternal Ends of ribs bulge (Rachitic Rosary Beads)
- Bowed Legs (Genu Varum)

◦ Dx → Rickets

- Rickets is characterized by **Vitamin D deficiency**
 - **Decreased** calcium & Phosphorus intestinal absorption → **increased PTH**
 - Causes **increased** osteoblast stimulation & expression of RANK-L → binds to RANK Receptor on osteoclasts → **increased Osteoclast activity**
 - **Increased** resorption & **decreased** supply of calcium & phosphate → **defective mineralization of bone** → **Accumulation of osteoid (unmineralized bone matrix)**

◦ Features:

- **Skeletal Deformities & Frontal Bossing**
- Flattened back of skull
- Muscle Weakness
- **Defects in teeth enamel**
- **Chest groove** (Pectus excavatum)
- **Subcostal groove** (Harrison's grooves)
- **Sternal Ends of ribs bulge** (Rachitic Rosary Beads)
- Bowed Legs (Genu Varum)

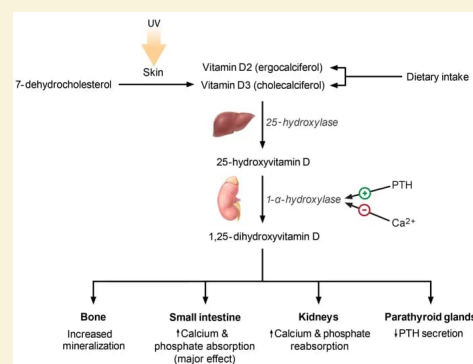


? Vitamin D deficiency due to decreased sun exposure is characterized by decreased production of what precursor?

▼ Answer

Cholecalciferol

- Body synthesizes **7-dehydrocholesterol** & deposited in the skin → UV exposure catalyzes conversion of **7-dehydrocholesterol to Cholecalciferol (Vitamin D precursor)**
- Cholecalciferol is then carried to the **liver** for **hydroxylation into 25-OH-Cholecalciferol via 25-hydroxylase**
- 25-OH-Cholecalciferol is then carried to the **kidney** for **hydroxylation into 1,25-OH-Cholecalciferol via 1-alpha-hydroxylase**



? What is the 2nd messenger does Vitamin D use?

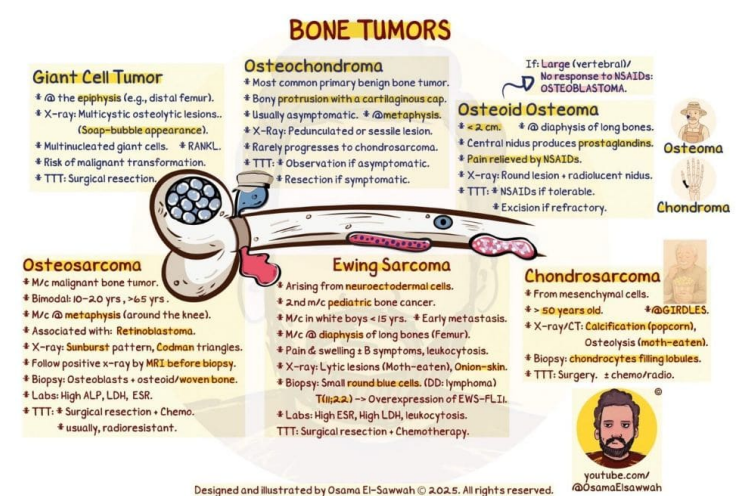
▼ Answer

Intracellular/Intranuclear Receptors - USMLE can refer to this as **"Binds to receptors in cytoplasm with translocation into the nucleus"**

▼ Other Choices

- **Choice A → Achondroplasia**
 - **AD; FGFR3 mutation**
 - Causes **abnormal Endochondral ossification** with disorganized or absent growth plates
 - Short Limbs with normal Head & Thorax
- **Choice B → I don't think there is something as ABSENT osteoblasts**

- **Choice C → describes Paget's disease (HY)**
 - Labs = All normal; **ALP high**
 - Phases = 3
 - 1) Lytic (increased number & activity of osteoclasts = increased bone resorption)
 - 2) Mixed (Increased activity of osteoblast & osteoclasts = Woven hypervascularized bone [not normal lamellar])
 - 3) Sclerotic (Decreased Osteoclast & Osteoblast activity)
 - **C/P = Bone Pain, Skull enlargement, CN 8 deficits "tinnitus"**
 - XRAY = Both lytic & Sclerotic lesions; Cortical thickening of vertebral endplates **"Picture-Frame Vertebrae"**
 - USMLE likes to give you bone pain + normal labs with high ALP & ask about Dx or gives you a vignette with a man with a hat that doesn't fit him anymore + tinnitus
- **Choice D → Osteosarcoma**
 - Site: Metaphysis
 - X-RAY: Raised periosteum (**Codman Triangle**) & **Sunburst appearance**
 - Biopsy: Osteoblasts & Osteoid / Woven bone
 - **HY → Associated with Retinoblastoma**



Q40

A 50-year-old woman is admitted to the hospital because of a 3-day history of nausea, vomiting, and upper abdominal pain that radiates to her back. She was diagnosed with HIV infection 3 months ago and has been adherent with her antiretroviral medication regimen. Her CD4+ T-lymphocyte count is 400/mm³ (N≥500), and plasma HIV viral load is 50 copies/mL. She appears acutely ill and diaphoretic. Her temperature is 36.8°C (98.2°F), pulse is 135/min, respirations are 30/min, and blood pressure is 95/55 mm Hg. Physical examination shows epigastric tenderness, abdominal distention, and absent bowel sounds. Results of laboratory studies show serum amylase activity of 450 U/L. The most likely cause of these findings is an adverse effect of which of the following drugs?

- A. Abacavir
- B. Acyclovir
- C. Didanosine (ddI)
- D. Lamivudine (3TC)
- E. Ribavirin
- F. Zidovudine (AZT)

▼ **Explanation**

- **Answer is C (Didanosine)**
 - **IMP Clues:**
 - HIV patient with low viral load & acceptable CD4 count (he takes his HIV drugs)
 - Amylase 450 U/L (pancreatitis most likely from his HIV drugs)

HIV DRUGS ARE SUPER HY ([watch this Dirty Medicine Video](#)) + has some great mnemonics too

- HIV drug that causes pancreatitis → **Didanosine**
 - NRTI Side-effects in general:
 - **Lactic Acidosis**
 - **Bone Marrow Suppression**
 - NRTI are “Nucleoside Reverse Transcriptase Inhibitors” that **inhibit synthesis of viral DNA [asked on NBME]**
 - How?
 - Normally, RNA is made from DNA (This is called Transcription)
 - However, **Reverse Transcriptase does the opposite → DNA is made from RNA**
 - So, **NRTIs cause inhibition of Viral DNA Synthesis**

? What NRTIs are associated with Peripheral Neuropathy?

▼ Answer

Didanosine, **Stavudine**, and **Zalcitabine** are the NRTIs that cause peripheral neuropathy

▼ Other Choices

- **Choice A → Abacavir** is a NRTI
 - causes hypersensitivity in patients who are **HLA-B5701**.
 - USMLE will ask what to do before starting abacavir? → HLA-B5701 testing
- **Choice B → Acyclovir** is a **DNA polymerase inhibitor of HSV & VZV. [asked on NBME]**
 - Most imp side effect for the USMLE is Crystal Nephropathy.
 - USMLE also likes asking what causes VZV / HSV resistance to acyclovir? → **Altered thymidine kinase**
- **Choice D → Lamivudine** is a NRTI with no specific side-effects
- **Choice E → Ribavirin** on the USMLE has 2 MOAs
 - **IMP dehydrogenase inhibitor**
 - **Ribonucleotide Reductase inhibitor**
 - Theoretically can help in ttt of RSV but NEVER the correct answer on the USMLE
- **Choice F → Zidovudine is a NRTI that is the MOST KNOWN for Bone Marrow Suppression on the USMLE [asked on NBME]**

Q41

During an experiment, an investigator observes that glutamate depolarizes cells through both N-methyl-D-aspartate (NMDA) and non-NMDA receptors. She finds that the initial depolarization phase of a glutamate-induced fast excitatory postsynaptic potential is generally mediated by activation of non-NMDA-type glutamate receptors rather than NMDA-type glutamate receptors. Which of the following best explains this finding?

- NMDA receptors are blocked by Mg^{2+} at the resting membrane potential
- NMDA receptors are more permeable to Ca^{2+}
- NMDA receptors can be activated only if the cell membrane is hyperpolarized
- Non-NMDA receptors are more permeable to Ca^{2+}
- Non-NMDA receptors are permeable only to Na^{+}
- Non-NMDA receptors have faster gating kinetics at the resting membrane potential

▼ Explanation

- Answer is A (NMDA receptors are blocked by Mg^{2+} at the resting membrane potential)
 - **IMP Clues:**
 - Glutamate depolarizes cells through NMDA & non-NMDA receptors
 - Initial depolarization phase is activated by non-NMDA receptor rather than NMDA (so we know eventually both get activated; however, the non-NMDA gets activated first)
 - **Explanation:**
 - This Q tests the knowledge of NMDA & AMPA (Non-NMDA Receptors)

- Normally AMPA & NMDA are present on the same synapse. Glutamate activates both however NMDA is blocked by Mg until sufficient AP is reached
- So, the initial Glutamate that attaches to AMPA causes Na influx & causes AP
- If enough AP occurs, AMPA single handedly depolarizes the membrane & kicks of the Mg ion off the NMDA channel.
- NMDA is now activated with the pre-placed glutamate & causes massive influx of Na & Ca

▼ Other Choices

- **Choice B** → is correct but does not explain this phenomenon
- **Choice C** → is incorrect because NMDA is active during depolarization NOT hyperpolarization
- **Choice D** → is incorrect because NDMA not non-NMDA is more permeable to Ca
- **Choice F** → is correct but the main reason is the presence of Mg not the faster gating kinetics

Q42

A 55-year-old African American man with hypertension is asked by the public relations representative of a hospital if he will allow filming of his next visit with the physician for a future broadcast designed to raise public awareness of hypertension. After full disclosure of the plan, the patient consents to filming and broadcasting. Immediately after filming is completed, the patient tells the physician that he does not want his medical condition made public. Which of the following is the most appropriate response by the physician?

- A. Ask the patient why he consented in the first place if he had concerns
- B. Explain to the patient the importance of raising social awareness of treatable medical conditions
- C. Explain to the patient that his consent cannot be rescinded at this point since the filming is completed
- D. Tell the patient that he can change his mind about participating
- E. Tell the patient that he will have to speak to the hospital public relations representative to cancel his participation

▼ Explanation

- Answer is D (Tell the patient that he can change his mind about participating)
 - **A VERY HY CONCEPT for ethics:** Patients who participate in a clinical trial or any activity (like a broadcast here) can withdraw from the said activity immediately and without any questions.
 - In simple terms: If he wants out, then he is out. No questions asked.

Q43

A 44-year-old man comes to the physician because of increasingly severe pain and swelling of his knuckles and knees during the past month. Physical examination shows tenderness, swelling, and warmth of the involved joints. Laboratory studies show an increased erythrocyte sedimentation rate and serum rheumatoid factor. The patient improves clinically after treatment with ibuprofen for 2 weeks. Which of the following sets of findings in plasma is most likely after 2 weeks of this therapy?

Choices	Leukotriene C4	Arachidonic Acid	Prostaglandin H2	Prostaglandin E2
A	Increased	Increased	Increased	Decreased
B	Increased	Increased	Decreased	Decreased
C	Increased	Decreased	Increased	Decreased
D	Increased	Decreased	Decreased	Increased
E	Decreased	Increased	Decreased	Decreased
F	Decreased	Decreased	Increased	Increased
G	Decreased	Decreased	Increased	Decreased

▼ Explanation

- Answer is B
 - **IMP Clues:**
 - Patient with Rheumatoid Arthritis treated with ibuprofen (an NSAID)

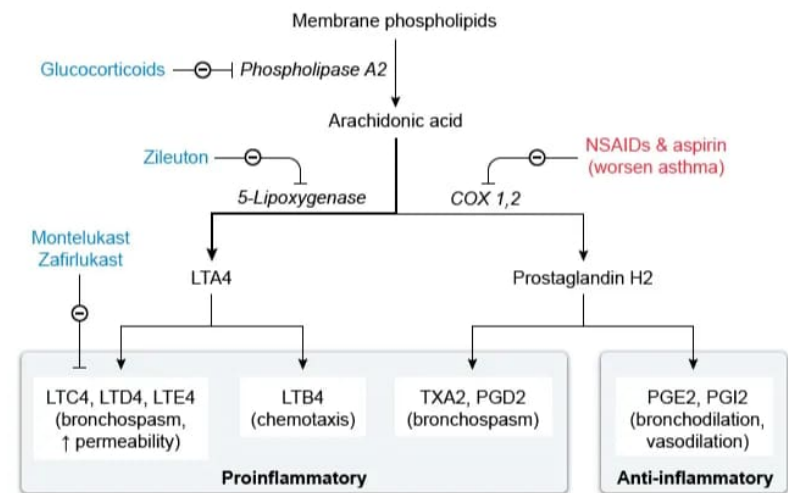
- NSAIDs

- NSAIDs are **COX inhibitors**, which cause:

- **Decreased Prostaglandins**
- **Increased Arachidonic acid level**
 - Shunting into Leukotrienes pathway → **Increased Leukotrienes**

- **So, answer is:**

- **Increased LTC4**
- **Increased Arachidonic Acid**
- **Decreased PGH2**
- **Decreased PGE2**



Phospholipase A2 is inhibited by **Corticosteroids**



What is Samter's Triad?

▼ **Answer**

Samter's Triad (Nasal Polyps, Aspirin-Induced Asthma - Aspirin-Induced Hypersensitivity) is assessed on the USMLE:

- Aspirin intake blocks PGs synthesis so all the arachidonic acid is shunted into Leukotrienes → most of them cause bronchoconstriction → Asthma in susceptible patients
- Treatment with **Zileuton** (5-LOX inhibitor) or **Montelukast & Zafirlukast** (Leukotrienes Receptor antagonists)



Selective vs NON-selective COX inhibitors:

NSAIDs/Aspirin are non-selective COX (1 & 2) Inhibitors

- **NSAIDs:** reversible & competitive antagonist of COX
- **ASPIRIN:** **IRREVERSIBLE & NON-COMPETITIVE** ANTAGONISM of COX

Celecoxib is a selective COX-2 Inhibitor, which can be used in people with Gastric Ulcers unlike normal nonselective NSAIDs

- **COX 1** → responsible for integrity of gastric mucosa & TXA2 formation (causes PLTs aggregation)
- **COX 2** → responsible for inflammation & VD

USMLE asks why physicians worry about using Celecoxib in patients who have Cardiovascular / Cerebrovascular diseases?

Answer is → HIGHER RISK OF THROMBOSIS

- Inhibiting COX2 causes VC
- Intact COX1 causes PLT aggregation 2ry to TXA2
- VC + PLT aggregation → yah not good.



LTB4 is a chemotactic molecule (attracts neutrophils to inflammation site)

- Chemotactic Molecules on the USMLE are: **C5a - LTB4 - IL-8 - PAF - Kallikrein**

All other Leukotrienes are involved in bronchoconstriction/asthma pathogenesis (There is NO Leukotriene F) [asked on NBME]

Q44

An 8-year-old girl is brought to the physician for a well-child examination. Her mother says that she has been well except for an occasional cold. Her immunizations are up to date. She is at the 50th percentile for height and 60th percentile for weight. Physical examination shows breast bud development and a few pubic hairs. The mother asks whether her daughter's development is normal. Which of the following is the most appropriate initial response by the physician?

- "I am concerned that your daughter may have precocious puberty."
- "I think that your daughter is likely to begin menstruating in the next few months."
- "I would like to order laboratory studies to ensure that your daughter's development is normal."
- "Your daughter's breast development is somewhat less than might be expected for her age."
- "Your daughter's development is normal."

▼ Explanation

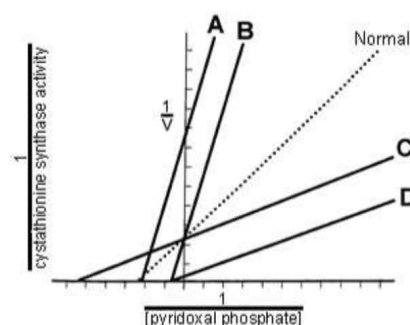
- Answer is E ("Your daughter's development is normal.")
 - IMP Clues:
 - Good medical hx + Up to date immunizations
 - 50th percentile for height & 60th for weight (you make think this is not normal; however, it is. If the percentiles are not VERY LOW or not far apart (for example, weight is 70th while height is 30th) then the kid is fine)
 - Breast Bud & few pubic hairs (just beginning puberty)
 - Dx → NORMAL DEVELOPMENT
 - Puberty starts at 8-11 years in girls so she's fine

What else do you need to know about puberty for STEP 1?

1. **First Objective Sign of Puberty in females is Thelarche (Breast bud development), and Testicular enlargement in males.**
2. **In girls, puberty starts at age 8-11**, so if a mother came to you with her daughter, which upon examining her found **breast bud & few pubic hairs** in these years, then **SHE IS NORMAL**.
3. **Bilateral gynecomastia** (can be described as **tender breast in a teenage boy**) is **NORMAL** and requires no intervention. **Follow-up** will be the answer to these Qs.
4. Puberty causes surge in androgens level, which **stimulate apocrine glands** in the armpits & groin ⇒ **Source of the sweaty, bad odor.**

Q45

A 5-year-old boy who has homocystinuria improves with high-dose oral pyridoxine therapy. Cystathionine synthase activity is 95% deficient in his cultured fibroblasts, but activity increases to normal after the fibroblasts are incubated with higher concentrations of pyridoxal phosphate. When cystathionine synthase activity is measured in the presence of pyridoxal phosphate, which of the following Lineweaver-Burk plots would be most consistent with this patient's findings compared with the kinetics of the enzyme in a normal individual?



- A. A
- B. B
- C. C
- D. D

▼ Explanation

- Answer is B
 - General Pharm is not that HY on USMLE but bear with me
 - First you need to know 2 very simple concepts
 - **K_m** → tells you about the **affinity** of the enzyme to its substrate (how much substrate is needed for the enzyme to work at 50% speed)
 - so, $K_m = 1/\text{affinity}$.
 - The higher the affinity, the lower the K_m
 - The lower the affinity, the higher the K_m
 - **V_{max}** → tells you about the **efficiency** of the enzyme (how well the enzyme catalyzes the reaction)
 - The higher the V_{max} , the more / the faster the enzyme is
 - The lower the V_{max} , the lower / the slower the enzyme is
 - So knowing these concepts, let's look at the given stem:



I use the stupid mnemonic "**AFK**" to remember

- **AF** = Affinity
- **K** = K_m

- we have an enzyme deficiency that IMPROVES with HIGH dose oral vitamin B6 (so the issue here is with the affinity. The HIGHER the concentration needed, the lower the affinity of the enzyme → the higher the K_m)
 - Activity increases to normal after they are incubated with higher concentration of vitamin B6 (SO when B6 concentration increases, V_{max} returns to normal; So, they have to intersect in the graph, so answer is either B or C)
- With these points in mind (we are nearly there believe me):
- In relation to normal, this patient has same V_{max} and lower K_m . How would this appear on the plot?
 - Same V_{max} = same Y-intercept (so either B or C)
 - Higher K_m = The higher the X-intercept (B is closer to 0, while C is in the negatives. B is higher)

Q46

A 52-year-old man is brought to the emergency department 30 minutes after the sudden onset of substernal chest pain. The pain has persisted despite self-administration of three doses of sublingual nitroglycerin. His pulse is 90/min, and blood pressure is 114/70 mm Hg. Physical examination shows diaphoresis. The lungs are clear to auscultation. Cardiac examination shows an S4. An ECG shows ST-segment elevation in the inferior leads. Intravenous morphine is administered, and he develops generalized pruritus and warmth 1 minute later. His pulse now is 120/min, and blood pressure is 90/50 mm Hg. Physical examination shows facial flushing. Which of the following substances is the most likely cause of the new symptoms and findings in this patient?

- A. Epinephrine
- B. Histamine
- C. Nitric oxide
- D. Serotonin
- E. Thromboxane A2

▼ Explanation

- Answer is B (Histamine)
 - IMP Clues:
 - Morphine administration followed immediately by generalized Pruritis & warmth (must be a morphine-induced side effect of some sort)
 - BP is 90/50 (hypotension due to VD) + Facial flushing (from VD)
 - Dx → Morphine induced Mast cell degranulation

IT IS SO HY TO KNOW THAT USMLE TESTS 2 VERY IMP CONCEPTS:

1. Mast cell degranulation (ASSOCIATED with Pruritis & Urticaria)

- IgE-mediated mast cell degranulation (examples are *atopy* & *eczema*)
- Direct-mast cell degranulation (most common examples are *morphine* & *Vancomycin* & *IV Contrast*)

2. Bradykinin Mediated (NOT ASSOCIATED with Pruritis & Urticaria)

- ACEi induced - accumulation of Bradykinin due to inhibited ACE that normally degrades the Bradykinins
- Hereditary Angioedema (C1 esterase inhibitor deficiency)



Bradykinin accumulation caused by ACE inhibitors is **NOT** caused by ARBs too.



Hereditary Angioedema is treated with **Danazol**

- Danazol increases C1 esterase **inhibitor** production from liver



Patient got a vancomycin injection & started flushing + developed hypotension. What is the Diagnosis & Treatment?

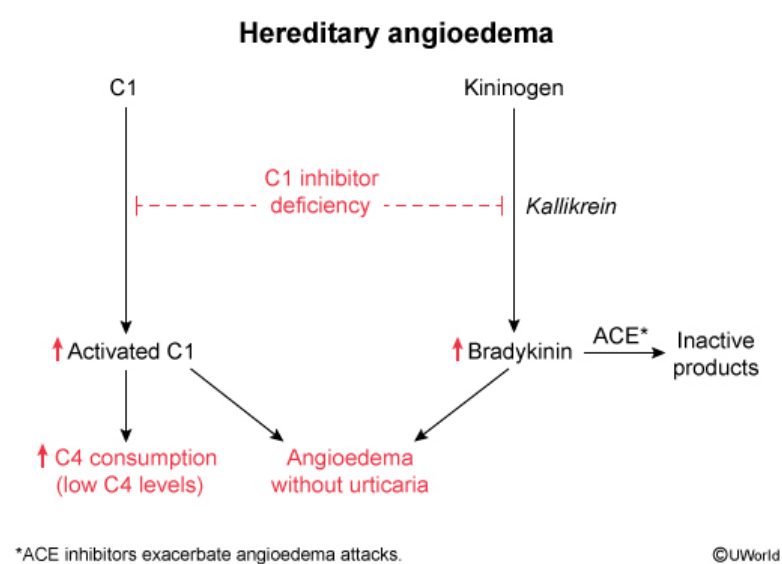
▼ Answer

Diagnosis is **Red Man Syndrome**

- Caused by **Direct-mast cell degranulation**

Treatment is with **Antihistamines**

- Vancomycin causes direct-mast cell degranulation → histamine release
- Histamine is the molecule causing the VD (Flushing & hypotension)
- So treated with antihistamines



Q47

A 24-year-old woman with sickle cell disease comes to the physician because of malaise and generalized fatigue for 1 week. She had previously felt well since her last sickle cell crisis more than 1 year ago. She has had no pain. Physical examination shows no abnormalities. Her baseline hematocrit is usually 25% to 30%. Laboratory studies now show a hematocrit of 13%, mean corpuscular volume of 105 μm^3 , and reticulocyte count of less than 1%. Which of the following diagnostic tests is most likely to explain this patient's symptoms and decreased hematocrit?

- A. Direct antiglobulin (Coombs test)
- B. Hemoglobin electrophoresis
- C. Measurement of serum haptoglobin concentration
- D. Serum parvovirus B19 IgM antibody test
- E. Bone marrow biopsy with examination of iron stores

▼ Explanation

- Answer is D (Serum ParvoB19 IgM antibody test)

◦ IMP Clues:

- Hx of Sickle cell disease (Parvo in sickle cell causes aplastic anemia, while in normal population is usually subclinical in the form of arthralgia especially in adults)
- Malaise & generalized fatigue (hints to anemia)
- No pain (not a sickled RBC, causing ischemia and pain to (most commonly) limbs)
- Dropped Hb (anemia) + high MCV (don't get tricked into thinking B9/B12 deficiency. This is merely because in cases of increased hemolysis, more B9 is needed to reciprocate for the increased demand of erythropoiesis) + Low retics (BM failure)

- Dx → Parvovirus- induced aplastic anemia in Sickle Cell patient

- Infects **erythroid precursor cells in bone marrow** & causes **interruption of erythrocyte production, resulting in Transient Aplastic Anemia [asked on NBME]**

- Usually asymptomatic / mild in healthy children, but can be life-threatening in children with **sickle cell anemia/Thalassemia/Hereditary Spherocytosis → Aplastic Crisis**

- Other HY Presentation of Parvovirus:

- **Erythema Infectiosum (Fifth Disease):** Presents as Slapped Cheeks rash in children, that then descends causing a lacy reticular rash.
- **Hydrops Fetalis:** TORCH infection in pregnant women.
- **Simple Arthralgia:** in adults.



USMLE Can give you a picture similar to the one above, so know how the reticular/lacy rash looks like:



Parvovirus is the **SMALLEST DNA virus** known!



Characteristics of Parvovirus?

▼ **Answer**

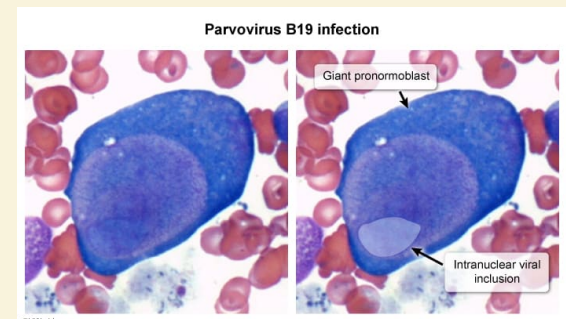
Single-Stranded DNA Naked Virus



What is expected to be seen on BM aspiration of this patient?

▼ **Answer**

Giant Pronormoblasts (shown below; a similar picture was on NBME 7, so worth knowing)



▼ **Other Choices**

- **Choice A → Coomb's test** is for Autoimmune Hemolytic conditions (like AHA)
- **Choice B → Hemoglobin Electrophoresis** is used to diagnose Thalassemia / Sickle cell anemia (already diagnosed)
 - alpha thalassemia = normal hemoglobin, while beta thalassemia has increase HbA2 & HbF
- **Choice D → Measurement of Serum haptoglobin concentration** is used to determine the presence of hemolysis: Increased hemolysis = increased Hb floating around = decrease available haptoglobin (less available because if it binds Hb, then it is not available anymore so level decreases)
- **Choice E → BM biopsy with examination of Iron stores** is the Golden Standard of diagnosing IDA (NOT used in clinical settings due to its invasiveness and the availability of easier / less invasive solid investigations)

Q48

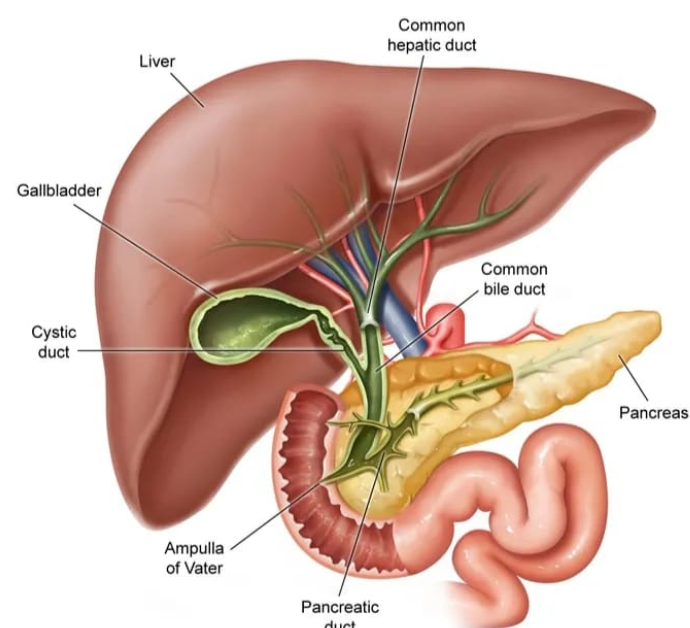
A 45-year-old woman comes to the emergency department because of a 1-week history of severe abdominal pain. She has a history of gallstones. Current medications are atorvastatin and hydrochlorothiazide. Her temperature is 37.2°C (99.0°F), pulse is 70/min, respirations are 20/min, and blood pressure is 130/90 mm Hg. Abdominal examination shows tenderness to palpation. Serum studies show increased activities of amylase and lipase. A CT scan of the abdomen shows enlargement of the pancreas and dilation of the pancreatic ducts. The most likely underlying cause of these findings is a gallstone lodged in which of the following locations in this patient?

- A. Bile duct (common)
- B. Common hepatic duct
- C. Cystic duct
- D. Hepatopancreatic ampulla
- E. Second part of the duodenum
- F. Uncinate process

▼ **Explanation**

- **Answer is D (Hepatopancreatic ampulla)**
 - **IMP Clues:**
 - Hx of gallstones (we know it is most likely a stone that recurred)
 - Increased amylase & lipase (Pancreas affected / inflamed)
 - CT scan showing enlarged pancreas + dilation of pancreatic ducts (something obstructing the pancreatic ducts distally, so it dilates)

- Dx → Pancreatitis 2ry to a stone in the Ampulla of Vater
 - Increased Serum Amylase AND Lipase ⇒ **Pancreatitis**
 - With the hx of gallstones, we can figure out that probably a stone escaped the GB → Cystic Duct → Common Bile Duct → Ampulla of Vater (Guarded by the Sphincter of Oddi)
 - CT scan showing "enlargement of pancreas & dilation of pancreatic ducts" tells us that there is an obstruction **distally**.
 - The Ampulla of Vater is the narrowest point along the distal portion of the biliary system, so it the **most likely site for stone obstruction**



? What enzyme is responsible for the pain in biliary colic?

▼ Answer
CCK

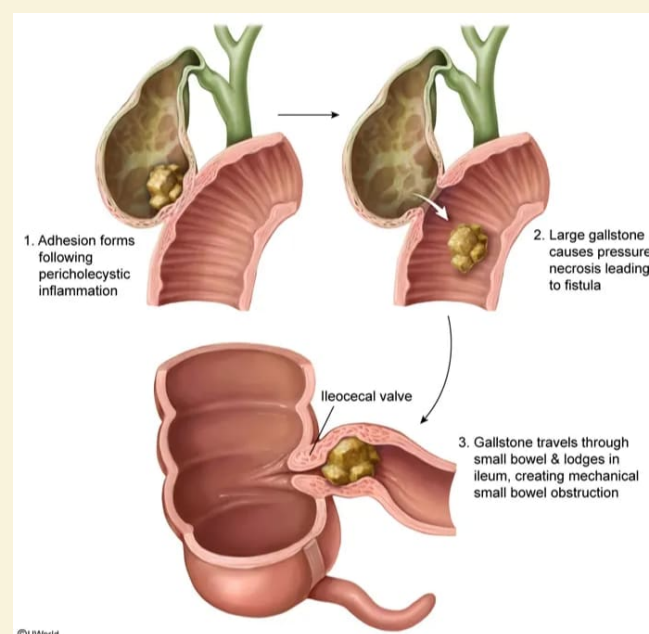
📌 45F + hx of RUQ colicky pain after fatty food + suddenly develops abdominal pain + distension + tympanic percussion on abdomen + U/S shows pneumobilia. What is the Dx?

▼ Answer

Gallstone Ileus

- Inflammation of recurrent cholecystitis causes a **cholecystoenteric fistula**, allowing gallstones to enter the intestines.
- Gallstones then lodge into the **ileocecal valve** (narrowest point in GI tract), causing an obstruction.

| **Pneumobilia** is enteric gas within the biliary system



▼ Other Choices

- **Hepatic duct, Cystic Duct, and CBD** stones would not cause the pancreas to dilate as they are above the level of the pancreas. They will cause dilation of what's before them. E.g.
 - **Choice B** → Hepatic duct stone would cause intrahepatic biliary dilation.
 - **Choice C** → Cystic duct stone would cause a dilated Gallbladder.
 - **Choice A** → CBD stone would cause a dilated intra & extrahepatic biliary ducts (above level of stone)
- **Choice F** → **Uncinate process** is just unrealistic answer
- **Choice E** → **2nd part duodenum** is less likely to occur as it is a large intestinal segment when compared to the biliary system.

Q49

A 9-year-old boy has mild mental retardation and a 4-year history of increasingly frequent major motor seizures. Physical examination shows normal vital signs, clear lungs, a moderate systolic ejection murmur, and discrete pink-to-yellow papules in a butterfly distribution on the bridge of his nose, the malar prominences, and along his nasolabial folds. A CT scan shows multiple, occasionally calcified nodules on the crests of some gyri in the subependymal regions. Echocardiography shows left ventricular hypertrophy associated with marked narrowing of the aortic valvular outflow tract due to a subvalvular mass arising from the septum. Which of the following is the most likely diagnosis of the cardiac lesion?

- A. Glycogen storage disease
- B. Hypertrophic cardiomyopathy

- C. Leiomyosarcoma
- D. Myxoma
- E. Rhabdomyoma

▼ Explanation

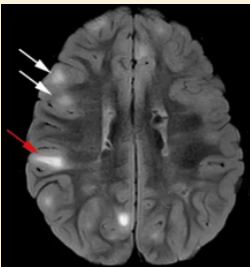
- Answer is E (Rhabdomyoma)
 - IMP Clues:
 - mental retardation + seizures + calcified nodules on gyri (Tubers: periventricular nodules)
 - papules on face (angiofibroma)
 - mass from septum causing valvular outflow tract (Cardiac Rhabdomyoma)
- Dx → Tuberous Sclerosis
 - AD; Neurocutaneous disorder
 - TSC1/TSC2 (Hamartin/Tuberin) gene mutation on chromosomes 9 & 16, respectively.

📁 TSC2 (Two) = Tuberin = sixTeen

- HY Features include:
 - Tubers “Periventricular Nodules” (causes seizures, here it caused the staring spells & mental retardation/Autism)
 - Ash-Leaf spots (Hypopigmented lesions)
 - Shagreen patches (Hyperpigmented lesions)
 - Cardiac rhabdomyoma (can present on the USMLE as a ball-in-valve murmur that disappears when patient is repositioned or child with obstructive symptoms)
 - Renal angiomyolipoma
 - Others: Angiofibromas & Subungual fibromas

? What are TSC1/TSC2?
▼ Answer
Tumor Suppressor Genes

 Tuberous Sclerosis
Buzzy Features:
Periventricular Nodules:



Shagreen Patches:



Ash-Leaf Spots:



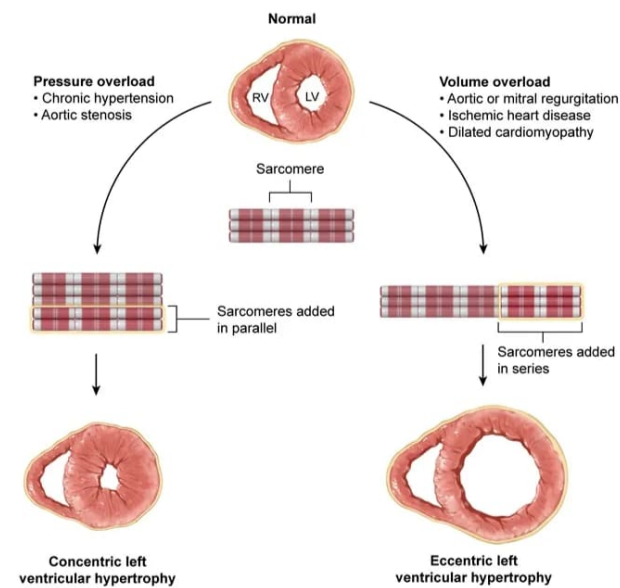
▼ Other Choices

- Choice D → Myxoma is found in adults & presents as a Left atrial mass that causes Obstructive shock & attacks of syncope.

 Myxoma presents in kids in ONLY ONE SYNDROME: Carney Complex

- Child with Hyperpigmentation (usually peri-oral melanosis similar to Peutz-Jeghers Syndrome but will not mention the hamartomatous colonic polyps but ask about the cardiac lesion)
- Atrial Myxoma (the cardiac lesion)
- Endocrine Hypersecretion (usually Cushing's)

- **Choice B → Cardiomyopathy** presents in 2 ways on the USMLE
 - **Concentric** in increased **afterload** (cardiac fibers stacked in **parallel** not in series)
 - **Eccentric** in increased **preload** (cardiac fibers stacked in **series** not in parallel)
- **Choices A & C → GSD & Leiomyosarcoma** are irrelevant here



Q50

A 48-year-old man comes to the physician because of increasing bronzing of his skin, weakness, and fatigue during the past 3 months. Physical examination shows bronzing of the skin, hepatomegaly, and small testes. Serum studies show:

AST	increased
ALT	increased
Iron	increased
Transferrin saturation	increased
Ferritin	increased
Testosterone	decreased
Luteinizing hormone	decreased
Follicle-stimulating hormone	decreased

Which of the following best explains the findings in this patient?

- A. Ferrochelatase deficiency
- B. Increased erythropoietin production
- C. Increased intestinal iron absorption
- D. Ineffective erythropoiesis
- E. Transferrin deficiency

▼ Explanation

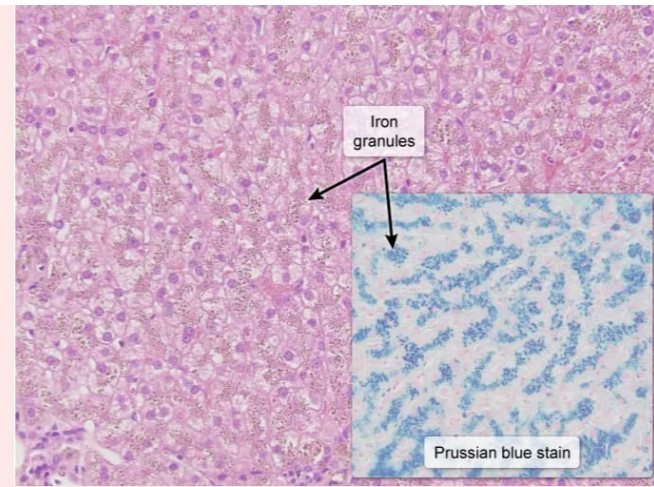
- **Answer is C (Increased intestinal iron absorption)**
 - **IMP Clues:**
 - Bronze skin (deposition of hemosiderin in skin)
 - Weakness & fatigue
 - Hepatomegaly + elevated enzymes (liver is affected)
 - Small testes + low FSH, LH, testosterone (hypogonadism)
 - Increased Ferritin & Iron (high iron load)
 - **Dx → Hemochromatosis:**
 - **AR**; mutation of **HFE gene** on **chromosome 6** causing “increased intestinal iron absorption” *[asked on NBME]*
 - Increased Iron absorption causes increased iron deposition all over the body
 - Iron overload causes:
 - **Deposits in skin → Hyperpigmentation / Bronze skin**
 - **Deposition in liver → Hepatitis & can progress to HCC**
 - **Deposits in tail of pancreas → DM & hypoglycemia**
 - **Deposition in joints → pseudogout (HY)**

USMLE loves giving you the below liver picture and asks for gene/mechanism/cause/complications:

- **Deposition in heart → *Cardiomyopathy* (Both dilated & restrictive cardiomyopathy)**
- **Deposition in testes, pituitary, hypothalamus → *hypogonadism & infertility***
- Diagnosis:
 - **Ferritin** > 300 ng/dl
 - **Transferrin** *decreased*
- Treatment:
 - **Serial Phlebotomy**



Treatment of Secondary Hemochromatosis "Transfusion Siderosis" is *iron chelation therapy* (Deferoxamine)



- Gene → **HFE mutation**
- Mechanism → **Increased Intestinal Iron absorption**
- Cause → **Iron overload & deposition into hepatocytes**
- Complication → **Hepatitis/Cirrhosis/HCC**



Why does hemochromatosis appear earlier in men than women?

▼ **Answer**

Women are able to excrete iron by menstruation. Men don't menstruate. I hope.

▼ **Other Choices**

- **Choice A → Ferrochelatase (and ALA dehydratase) deficiency** causes Lead poisoning
- **Choice B → Increased EPO production** is seen 2ry to chronic hypoxia (COPD) or with some tumors (RCC & HCC)
- **Choices D & E → Ineffective Erythropoiesis & Transferrin deficiency** are just nonsense here.
 - Ineffective Erythropoiesis is BM failure
 - Transferrin deficiency = low transferrin (in given labs transferrin sat is high)



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